JUN 30 1933

The Successful Promotion of Pharmacy Results Not Only from the Developed Capacities of Its Votaries, but Is Equally Dependent upon Their Active Coöperation. Share in the Activities of Your State and National Associations.

Vol. XXII, No. 6 JUNE, 1933

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 81st ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN MADISON, WISCONSIN, AUGUST 28 TO SEPTEMBER 2, 1933, HOTEL LORAINE, HEADQUARTERS, EMERSON STANLEY, 602 CENTRAL BUILDING, MADISON, LOCAL SECRETARY.

The 1933 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Madison.

Entered as second-class Matter, January 23, 1917, at the Post Office at Easton, Pa., under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in section 1103. Act of October 3, 1917; authorized July 10, 1918.

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Pharmacy Exhibit in the Smithsonian Institution, Washington. A large part of this collection was contributed by veteran member, J. U. Lloyd.

The State Capitol and Lake Monona in the background, Lake Mendota to the left with fraternity house piers extending into the Lake and some of the University buildings in the foreground.

The University of Wisconsin Campus, on the left with the State Capitol in the distance.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXII JUNE, 1933 No. 6

THE A. PH. A. MEETING AT MADISON.

PARTS OF A MESSAGE BY J. W. SLOCUM, CHAIRMAN, HOUSE OF DELEGATES.

IT HAS occurred to the writer time and again that the state pharmaceutical associations are not living up to their full privilege in respect to their relation to the parent organization—the AMERICAN PHARMACEUTICAL ASSOCIATION.

The House of Delegates is a division of the ASSOCIATION, in which the state associations have the majority of delegates. It provides a national forum for the consideration of the problems and progress of pharmacy.

It is true that most associations send delegates to the National meeting but too frequently it is considered a gracious gesture or privilege granted to an individual, rather than the thought that the delegates should bring back something of the inspiration and the aspirations of our profession.

One of the important purposes of the AMERICAN PHARMACEUTICAL ASSOCIATION is to render service to the state associations, hence, those in authority in the state associations should be present and absorb some of the enthusiasm, and suggestions for formulating workable plans for pharmacy in their own states during the ensuing year.

What an ideal representative body we would have at Madison if the president and secretary of every state association could be present. To them the members naturally look for a program of progress, and rightly so. The responsibilities that rest upon them are heavy and those in authority should see that they are given the opportunity of contacting the best brains in the field of pharmacy. We cannot conceive of pharmacists attending these meetings without receiving valuable suggestions and information which, if made operative in their own states, would assure a year of worth-while, creative effort. In past years, we have observed that strong associations are always well represented at the annual meetings of the AMERICAN PHARMACEUTICAL ASSOCIATION; in fact, that is one of the reasons why they have become strong. From these meetings they have received the incentive which, when expressed in terms of energy at home, has spelled success for them.

We cannot too strongly urge that this suggestion be given serious consideration in every state association, because we are firmly convinced that if the president and secretary of all state associations could be present each year at the annual convention of the AMERICAN PHARMACEUTICAL ASSOCIATION, it would contribute more to the success of pharmacy than any other one thing in which all pharmacists may share.

EDITORIAL

E. G. EBERLE, EDITOR 10 West Chase Street, BALTIMORE, MD.

FEDERAL FOOD AND DRUGS ACT.

THE bill providing for a new Federal Food and Drugs Act is now before Congress, but its enactment will not be possible until its next session. Some of the outstanding changes in the bill for the provisions of the present law applying to pharmacy, are:

Extension of jurisdiction to advertising; inclusion of cosmetics; provisions to control more adequately false or misleading therapeutic claims on drugs; requirement for fully informative labeling of drugs; more adequate remedial provisions.

Among definitions the term "drug" includes: (1) all substances and preparations recognized in the United States Pharmacopœia or National Formulary or supplements thereto; and (2) all substances, preparations and devices intended for use in the cure, mitigation, treatment or prevention of disease in man or other animals; and (3), all substances and preparations other than food, and all devices intended to affect the structure or any function of the body of man or other animals.

The term "cosmetic" includes all substances and preparations intended for cleansing or altering the appearance of, or promoting the attractiveness of the person. Except as indicated in the definitions of food, drug and cosmetic they shall not be construed as mutually exclusive.

Under the provisions of the bill a drug shall be deemed to be adulterated: If it is or may be dangerous to health under the conditions of use prescribed in the labeling thereof. If its name is the same as or simulates a name recognized in the United States Pharmacopœia or National Formulary or in any Supplement thereto, official at the time the drug is introduced into interstate commerce or if it purports to be such a drug and fails to meet the definition, formula and prescription set forth therein or differs from the standard of strength, quality or purity as determined by the tests or methods of assay set forth therein; except that whenever tests or methods of assay have not been prescribed therein or such tests or methods of assay are prescribed are found by the Secretary to be insufficient, he is hereby authorized to prescribe by regulations, tests or methods of assay for determining whether or not such drug complies with such standards. No drug shall be deemed to be adulterated if its label appears in the manner and form prescribed by regulations of the Secretary, a statement indicating wherein its strength, quality and purity differ from the standard of strength, quality and purity set forth in the United States Pharmacopœia or National Formulary, or in any Supplement thereto, official at the time the drug is introduced into interstate commerce, as determined by the tests or methods of assay applicable.

Further comment will be made from time to time on the measure because of its importance. This Act shall take effect six months after the date of approval; the present Act remains in force until that time.

THE FUTURE OF PHARMACY.

IN AN editorial by this writer a few years ago it was said that the thoughts and acts of the young men and women who during "Commencement Month" will

become accredited pharmacists will show the influence of those who have taught them.

It has been repeated for centuries that the problems of the day are more difficult than ever before; it was said by our forefathers and it will be said by those who now enter pharmacy. Those who preceded us solved some of the problems that were left to them, some were passed on to their successors. We have problems which disturb us; others are about to be solved and new ones are looming up before us; the difficulties they present point out our duties and give us opportunities; the solution or adjustment of them aids in our uplift and advancement in the better service for humanity. Throughout the world pharmacy has been grappling with big problems and in every country there has had to be readjustment to changed conditions. The history of pharmaceutical achievement of the last decade compares favorably with the accomplishments of the past half century and the story is being told at the Chicago World's Fair; what is wanted is constructive thought and action.

In discussing the Report on the Costs of Medical Care at the District No. 2 meeting of the members of the Boards of Pharmacy and of the College Faculties, in Philadelphia, Dean Hugh C. Muldoon said in part:

"Whatever may be our opinion of its worth and of its possible future influence, we cannot but be interested in those parts of the Report of the Committee on the Costs of Medical Care which touch directly or indirectly upon pharmaceutical education. We will all agree with the Committee that the safety of the public is paramount, and that the pharmaceutical educators should lose no opportunity to emphasize the pharmacist's responsibility for public health and safety. We believe, too, that the pharmacist must be well trained professionally, and we agree that he should have also a sound cultural and scientific background. The suggestion will commonly be approved that the pharmaceutical educational program should be more closely correlated with education in the other public health professions in order that pharmacists may be able to coöperate more intelligently and capably with workers in those fields."

An editorial of the *Australasian Journal of Pharmacy* closed with these words: "The call in pharmacy to-day is the will to adopt a plan and to stick to it until it is brought to a final and successful conclusion. There is much that cannot be done—there are forces that cannot be overcome by direct attack—but by means of flank attacks and concerted action by the whole body along definite lines the way can be paved to brighter and better things. The heritage of pharmacy lies in the traditions of the past. Its future depends on those who are practising its profession to-day. Great responsibility is cast on those who are leading in the van, but equally is the need on the part of all of the true coöperative spirit that is willing to sacrifice to some extent its individuality in order to gain a greater success for the good of all."

A PROPOSED STANDARD TABLE OF POISONS.

THE National Drug Trade Conference has undertaken the preparation of a reference list of drugs and chemicals which properly bear the poison label when dispensed otherwise than upon the prescriptions of physicians. It is a matter of

impossibility to form a definition for poison which will serve as an accurate guide in every case, hence this work is very timely and will meet a necessity long recognized. The Committee having this work in charge is composed of A. G. DuMez, S. L. Hilton, Robert L. Swain, A. C. Taylor and James H. Beal, *Chairman*. A tentative list has been prepared and is submitted with the express purpose of listing comment and criticism; it is published in this issue of the JOURNAL.

U. S. P. X INTERIM REVISION.

THE U. S. Pharmacopœial Convention for the revision of the United States Pharmacopœia X provided for interim revisions whenever deemed necessary. "Interim Revision Announcement" No. 1 has been issued under date of June 1, 1933, by Chairman E. Fullerton Cook, being a revision of the text and assays for "Ergot and Fluidextract of Ergot," also a revised test under Lactose. This revision becomes official January 1, 1934. The three groups responsible for the revision of this text—namely, the Sub-Committee on Botany and Pharmacognosy; the Sub-Committee on Extracts, Fluidextracts and Tinctures; and the Sub-Committee on Biological Assays—are continuing their investigations and it is expected that still other changes will be recommended for the U. S. P. XI.

GERMAN PHARMACY ORGANIZATION.

THE Deutscher Apotheker Verein (German Apothecaries Society) and other pharmaceutical societies have effected an organization—the Standes gemeinschaft, conforming to the program of the new National State. Included are all *qualified* pharmacists—retailers, wholesalers and those in the chemical and pharmaceutical industries. The *Pharmazeutische Zeitung* of April 29th comments at length on the organization, its aims and purposes and hopefully quotes lines from Schiller:

"Das Alte stürzt, es endert sich die Zeit, und neues Leben blüht aus den Ruinen." (In substance—The old falls, times change and new life blossoms out of the ruins.)

A decree issued on April 18th by the Prussian Government directs that all applications for admission of apprentices in a pharmacy are to be refused in view of alterations in the examination regulations in the near future. New legislation restricts pharmacy to those qualified, the Government controls proprietary preparations, makes unlimited free distribution of samples to physicians illegal.

The presentation of the organization plan in the publication referred to concludes by expressing hope for success, the welfare of the profession and the German people.

A comment in the *Pharmaceutical Journal and Pharmacist* on the new German Pharmaceutical organization states that "in the plan there are certain points which, if enforced, should excite the admiration and envy of British pharmacists."

We hope that the people will be better served, pharmacy enabled to render better service, its opportunities developed and productive of financial returns commensurate with the importance of the profession.

SCIENTIFIC SECTION

BOARD OF REVIEW ON PAPERS.—*Chairman*, L. W. Rowe; John C. Krantz, Jr.; F. J. Bacon.

THE PHARMACOLOGIC ACTIVITY OF CHEMICALLY ASSAYED SPIRIT OF ETHYL NITRITE, U. S. P., INCLUDING p_H VALUES.*

BY MARVIN R. THOMPSON,[1] MARVIN J. ANDREWS[2] AND CASIMER T. ICHNIOWSKI.[3]

INTRODUCTION.

In a recent communication, one of us (M. J. A. (1)) reported an extensive investigation of the chemical assay methods, and the stability of Spirit of Ethyl Nitrite prepared by various methods and placed under different storage conditions. The results of this work definitely confirmed earlier work that showed this preparation to be subject to loss of ethyl nitrite as shown by chemical assay, the rate of loss being dependent in large measure to the conditions under which the preparation was kept.

Although Spirit of Ethyl Nitrite is an exceedingly well-known preparation, being used therapeutically to a considerable extent, it appears that this preparation has never been subjected to a thorough pharmacological study, and indeed the various texts relating to pharmacologic action and therapeutic use seem hesitant to concede any significant action to this product. At least, we have been unable to find any satisfactory evidence which would recommend or condemn the preparation. A review of ten authoritative texts on pharmacology may be briefly summed up by stating that Spirit of Ethyl Nitrite is in all instances discussed simultaneously with the so-called "nitrite" series, and although other members of the series such as amyl nitrite, glyceryl trinitrate, sodium nitrite, erythrol tetranitrate, and mannitol hexanitrate have been investigated individually and comparatively, the Spirit of Ethyl Nitrite itself appears to have been quite neglected as far as any specific experimental investigation on this particular preparation is concerned. The present experiments were, therefore, undertaken in the hope of finding an answer to the following questions:

1. Is Spirit of Ethyl Nitrite, U. S. P. X, capable of exerting any significant activity whatever in its usual dosage and mode of administration?
2. Do the accepted chemical methods of assay reflect the pharmacologic potency in the deteriorated preparation, as well as when freshly prepared, or, do new products arise during deterioration which might result in pharmacologic activity even after chemical assay showed either partial or complete loss of activity?
3. In case of activity, does the nature and duration justify the existence of this preparation in the Pharmacopœia?
4. Is the p_H factor of any significance in this preparation?

EXPERIMENTAL METHODS.

Because of its position as a member of the "nitrite" series, and because of the therapeutic use as a vaso-dilator, diuretic, febrifuge and diaphoretic, we have in-

* Scientific Section, A. PH. A., Toronto meeting, 1932.

[1] Emerson Professor of Pharmacology, School of Pharmacy, University of Maryland.

[2] Assistant Professor of Pharmacy, School of Pharmacy, University of Maryland.

[3] Assistant in Pharmacology, School of Pharmacy, University of Maryland.

vestigated the activity qualitatively and quantitatively of freshly prepared and also deteriorated samples of U. S. P. X Spirit of Ethyl Nitrite by recording simultaneously upon both anesthetized dogs and cats, the carotid arterial blood pressure, respiration, kidney volume and urine output, in doses ranging from ineffective to lethal amounts, by intravenous, subcutaneous and oral administration.

(*a*) *Animals Used.*—Dogs, male and female, weighing from 6.0 to 13.0 Kg. Cats, male and female, weighing from 2.2 to 4.1 Kg.

(*b*) *Anesthesia.*—To avoid as much as possible the circulatory effects of anesthesia, our anesthesia was carefully maintained only to a depth necessary to abolish interfering voluntary movement, by the very slow intravenous injection of a just sufficient amount of sodium ethyl-methyl-butyl barbiturate (Nembutal).[1] As the anesthesia tended to wear off with the passage of time (single experiments occasionally lasting as long as seven hours), additional small amounts were given. This method, because of the rapidity of onset of anesthesia and the relatively short duration of effect of this hypnotic, makes it possible, with some experience, to control the anesthesia at any depth desired with an unusual degree of accuracy.

(*c*) *Operative Procedures and Methods of Recording.*—1. Carotid Blood Pressure. This was carried out in the usual manner.

2. Respiration. Respiration was recorded through a tracheal cannula to a suitable tambour recorder.

3. Kidney Volume. This was accomplished by very carefully dissecting out the kidney and placing around it an oncometer of proper size, closing the incision and taking the record through a tambour recorder. The sensitivity of our recording device was sufficiently great to record not only the kidney volume, but even the pulsations coming through the renal artery.

4. Urine Output. Urine flow was obtained, in the experiments upon dogs, by inserting a specially constructed Y-shaped cannula into both ureters at a point near the bladder. Because we were unable to insert a cannula of proper shape and size into the ureters of cats, a specially blown bladder cannula was tied into the bladder so as to receive the urine directly from both ureters, thereby avoiding a "lag" which results if the cannula is of improper shape or is not tied in properly. In either case, the urine flow was recorded through a Becker drop-recorder and signal magnet.

All four types of activity were recorded simultaneously upon a slow-moving kymograph.

(*d*) *Method of Administration of the Test Preparations.*—Since it was desired to evaluate different samples quantitatively as well as qualitatively, the preparations were administered intravenously for this phase of the work. To avoid the effects of irritation which would otherwise be caused by the high alcohol content of the spirit, a cannula fashioned on the order of a Hitchins' Syringe was employed, introduced into the femoral vein. This permitted "washing in" the desired dose with saline solution, without a loss of the highly volatile ethyl nitrite. Aqueous dilution of this preparation before administration is not permissible because of an evolution and loss of ethyl nitrite, thereby destroying the quantitative accuracy of the dose.

Since therapeutic use of Spirit of Ethyl Nitrite is permissible by oral administration only, because of the high alcohol content, it was necessary to also study the effects produced by oral administration. This was accomplished by using a small rubber stomach tube in the usual manner, washing the dose into the stomach with a little water.

In both oral and intravenous administration, control doses of alcohol were frequently given, to avoid improper interpretation of results.

The frequency of dosage was found to be very important from the quantitative standpoint. To avoid discordant results it was necessary to wait until the effects of the previous dose had worn off completely. The waiting time depended upon the size of the dose, and was determined simply by waiting until the carotid blood pressure had returned to normal.

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[1] We are indebted to the Abbott Laboratories for a generous supply of this material.

THE TEST SAMPLES OF SPIRIT OF ETHYL NITRITE EMPLOYED.

Since it was desired to ascertain whether the activity of the deteriorated preparations was identical in kind to that of the freshly prepared preparations of U. S. P. ethyl nitrite content, or whether deterioration or changes due to aging resulted in the formation of other active substances, it was necessary to compare the activity of samples having undergone varying degrees of deterioration with the activity of a freshly prepared preparation meeting all U. S. P. requirements.

Being impossible to illustrate our findings by a complete reproduction of all our experiments, we have decided to show in the following Table I the exact character of the test samples employed in producing those tracings reproduced in this article. Owing to the danger of deterioration, each sample was assayed on the morning of the same day of the pharmacologic tests, the assay values given being those found on the day of the tests.

The p_H values of the samples included in the table were determined potentiometrically by a capillary electrode method which we have found to be accurate and reliable, even when applied to highly alcoholic solutions. This method was briefly described in an earlier communication (2). Although the colorimetric method was also used, we were unable to procure satisfactory results by this method, owing to the properties of this preparation.

TABLE I.—DESCRIBING THE TEST SAMPLES EMPLOYED IN PRODUCING THE REPRODUCED KYMOGRAPH TRACINGS OF THIS REPORT.

Prepared by U. S. P. X Method.

Identification No.[1]	Ethyl Nitrite Content at Time of Mfg.,[2] %.	Age at Time of Pharmacologic Test, Months.	How Stored.	Ethyl Nitrite Content at Time of Pharmacologic Test, %.	p_H Value at Time of Pharmacologic Test.
1	4.25	Freshly prepared	Tight amber bottle in refrigerator	4.25	0.82
2	4.23	23	Tight amber bottle in refrigerator	2.59	0.46
3	4.23	23	As above in diffused sunlight, room temperature	1.54	1.00
4	4.23	23	Tight clear bottle, direct sunlight	0.00[3]	5.95
5	4.23	23	Same as No. 4	0.00[3]	4.34

[1] This number corresponds with that appearing on the tracings.

[2] U. S. P. X Method, replacing salt solution in nitrometer with mercury.

[3] Samples Nos. 4 and 5 had deteriorated completely when assayed after 13 days.

EXPERIMENTAL RESULTS.

Owing to the fact that the usual individual variations in the quantitative response of both dogs and cats were observed, and that the showing of the quantitative relationship between the test samples of Table I is a major purpose of this report, the accompanying tracings of experiments on dogs were obtained from one and the same dog, and likewise the tracings of experiments upon cats were obtained from one and the same cat. The results shown in these tracings are typical, and were reproduced on other cats and dogs repeatedly.—(*Continued on page 492.*)

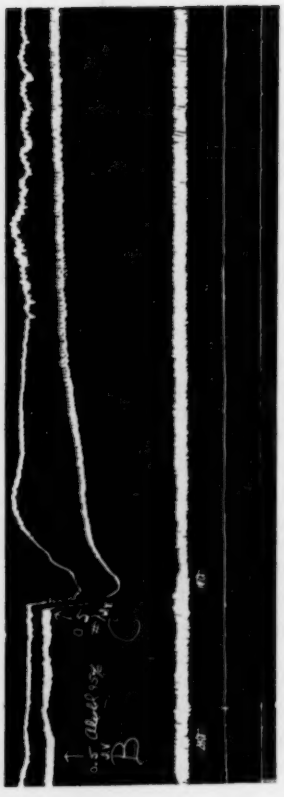

Plate I.

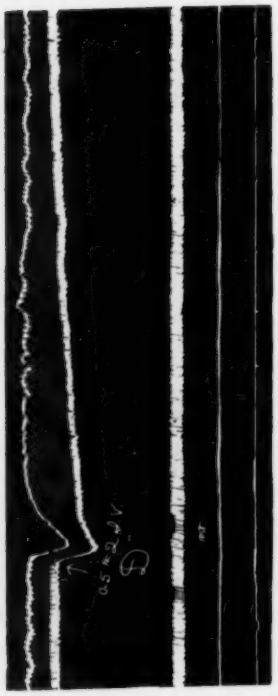

Plate II.

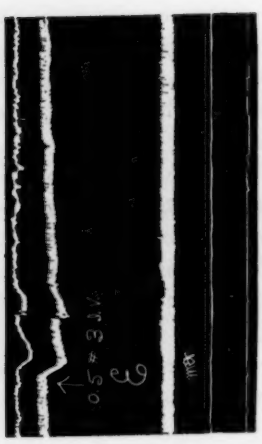

Plate III.

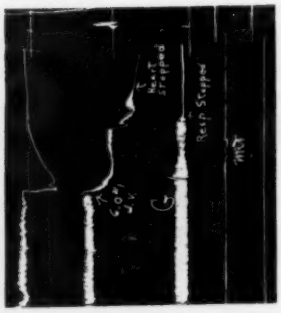

Plate V.

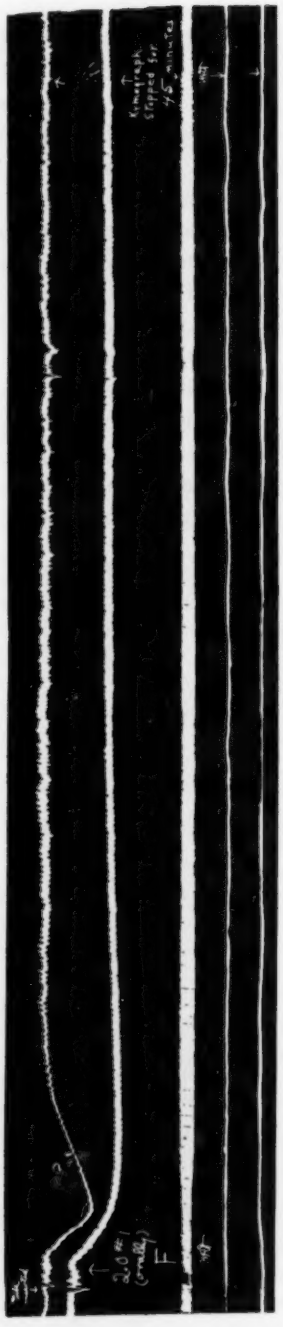

Plate IV.

EXPLANATION OF PLATES.

Plate I.—Dog, male, 12.0 Kg. Recording, from top to bottom, kidney volume, carotid blood pressure, respiration, time in minutes (about 1 cm. per minute) and urine flow in uniform drops. The negligible effect of a control dose of 0.5 cc. of 95% alcohol, washed into the femoral vein at B. At C, the effects of 0.5 cc. of sample No. 1 of Table I, washed into the femoral vein with saline. Note the prompt but transitory decreased kidney volume, prompt and persistent fall in blood pressure, transitory depression then prolonged stimulation of respiration, and a complete retention of urine for 15 minutes, after which the urine again begins to flow, but at a retarded rate. This preparation was of full U. S. P. strength, as shown in Table I, and was used as the quantitative standard of comparison.

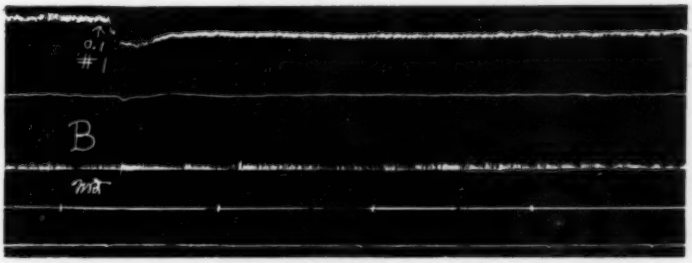

Plate VI.

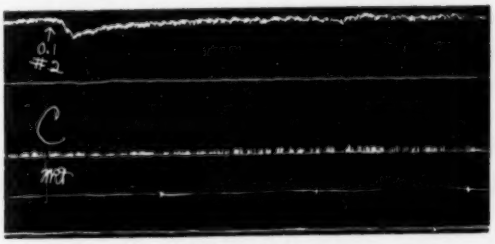

Plate VII.

Plate II.—A continuation of Plate I. At D, the same dose of sample No. 2 of Table I was given, as was given of sample No. 1 in Plate II. Note from Table I that sample No. 2 is approximately two-thirds of the strength of No. 1 in ethyl nitrite content, and that the pharmacologic response of all recorded functions in this figure is approximately two-thirds of that of Plate I.

Plate VIII.

Plate III.—A continuation of Plate II. At E, the same dose of sample No. 3 of Table I was given, as was given of sample No. 2 in Plate II, and sample No. 1 in Plate I. Note that the decreased response of all functions is proportional to the diminished ethyl nitrite content as shown by referring to Table I.

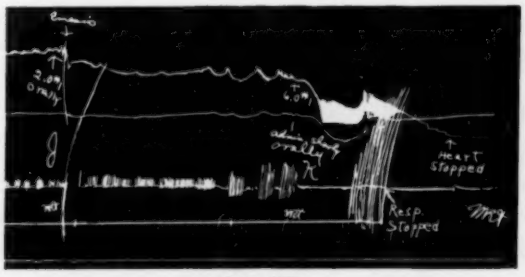

Plate IX.

Plate IV.—A continuation of Plate III. The effects produced by the oral administration at F of 2.0 cc. of sample No. 1 of Table I. This dose caused a fall in blood pressure which had not even started to return to normal in over two and one-half hours, when time necessitated termination of experiment. Note a complete retention of urine during the entire period. Also note the respiratory stimulation, and the prompt return of kidney volume to normal. The temperatures when the experiment was terminated was 4° C. below normal.

Plate V.—A continuation of Plate IV. 6.0 cc. of sample No. 1 was given intravenously at G. Note the continuation of heart beat after cessation of respiration, then death. Also note

return of kidney volume to normal before death, in spite of a continued fall in blood pressure.

Plate VI.—Cat, male, 3.3 Kg. Recording, from top to bottom, carotid blood pressure, kidney volume, respiration, time in 10-minute intervals, and urine output in uniform drops. At B, a dose of 0.1 cc. of sample No. 1 of Table I was washed into the femoral vein. Note the similarity of these effects to those shown in Plate I. They are less in magnitude, however, owing to the smaller dose per Kg.

Plate VII.—A continuation of Plate VI. At C, 0.1 cc. of sample No. 2 of Table I, which was approximately two-thirds of the potency of sample No. 1 given in Plate VII. Note the corresponding decrease in intensity of effects upon all functions recorded.

Plate VIII.—A continuation of Plate VII. Note the proportionately decreased effects produced by sample No. 3 of Table I. Note the absence of effects following the intravenous administration of 0.1 cc. of No. 3 at D, 0.1 cc. of sample No. 4 at E, and the same dose of sample No. 5 at F. As shown in Table I, these preparations were inert by chemical assay.

Plate IX.—A continuation of Plate VIII. The effects of oral doses of 2.0 cc. at J, and an additional 6.0 cc. at K. The heart continued to beat for over two minutes after respiratory failure. Here again, the kidney volume is seen to return to normal even while carotid blood pressure continued to fall. Urine flow interrupted as usual.

(*Continued from page 489.*)

Test preparation No. 1 of Table I was used in these tracings as the quantitative standard of comparison of activity.

The particular dog from which the indicated tracings were obtained was normal male weighing 12.0 Kg. The cat was a normal male weighing 3.3 Kg.

The rectal temperature was noted frequently on both cats and dogs during the course of the experiments.

DISCUSSION OF RESULTS.

There being no method of recording the temperature upon the kymograph at our disposal, a brief description of our observations is important. During the course of the various experiments, the temperature was observed to fall as much as 4° C. This was, of course, the result of several doses upon each animal. Our results showed that the fall in temperature was very roughly related to the size of the dose of ethyl nitrite (by chemical assay), and usually became apparent within a half hour after the dose was given.

Little other explanation of our results is necessary, but we would simply point out the following, which we believe is adequately shown by our results:

The effects observed upon cats and dogs were identical, and will, therefore, be briefly described without reference to either individually. The effects described are for non-toxic doses, unless otherwise stated.

EFFECTS UPON CAROTID BLOOD PRESSURE AND HEART.

This effect was typical of the members of the "nitrite" series. As shown in the tracings, single doses result in a prompt and extensive fall in blood pressure which is of a decidedly lasting nature, persisting for a period varying from a half hour to several hours, the magnitude and persistence depending upon the size of the dose. The effect upon the heart appears to be negligible, being only that secondary influence which is to be expected whenever the arterial blood pressure is materially lowered. A moderate acceleration was generally noted, due to the reflex stimulation caused by the fall in arterial pressure. The fall in blood pressure is due to vaso-dilation, since the heart is accelerated.

EFFECT UPON KIDNEY VOLUME.

As might be expected, the fall in blood pressure was always accompanied by a decrease in kidney volume. It is significant, however, that the kidney volume returned to normal within ten minutes, while the blood pressure remained low for many times this period. In other words, the effect upon kidney volume must be considered quite transitory, and, therefore, negligible in therapeutic employment.

EFFECT UPON RESPIRATION.

The larger intravenous doses produced a transitory respiratory depression, followed by mild, but definite and more prolonged stimulation, but the smaller intravenous doses and even relatively large oral doses produced the prolonged stimulation without the preliminary depression.

EFFECT UPON URINE OUTPUT.

With this effect, we encountered a distinct surprise. Contrary to the statements of several texts, a diuretic action was not observed in a single instance. A very distinct effect was always produced, but as is shown in the tracings, it was an antidiuretic effect, *i. e.*, as long as there was any evidence of effect upon blood pressure, or other recorded functions, there occurred simultaneously a decreased urine-flow in all experiments, and complete urine retention for appreciable periods when the larger doses were given. After the effects of the dose had worn off, it is true that the urine flow became accelerated, but the increased amount did not significantly exceed that which would otherwise have been excreted during the period of urine retention.

EFFECT UPON TEMPERATURE.

Although it is a well-known fact that it is very difficult to significantly lower the temperature of a normal animal, our observations have shown that Spirit of Ethyl Nitrite, U. S. P., is quite active in producing such an effect. A lowering of the rectal temperature of 1° C. was often observed, while the temperature during the course of several experiments fell 3° C. and even 4° C. In the latter case, administration of additional test doses was discontinued and after four hours the temperature had returned to within 1° C. of normal.

This would indicate that the employment of this preparation in febrile conditions (where all antipyretics exert their influence most readily) especially in children, almost invariably accompanied by a somewhat raised arterial blood pressure, is a distinctly rational procedure.

As to the mechanism of the antipyretic effect, we believe it to be due to both decreased heat production (decreased circulation and consequent decreased metabolism), and also increased heat loss (cutaneous capillary dilation and consequent increased radiation).

ACUTE TOXICOLOGICAL EFFECTS.

We have not attempted to accurately determine the M. L. D. of this preparation, but our results show a very safe latitude of therapeutic action. We have had to exceed ten times the minimum effective dose by a considerable amount in order to produce death, by oral administration as this preparation is ordinarily administered therapeutically.

When lethal amounts are given orally or intravenously to either cats or dogs, death is produced by respiratory failure, as shown in Plate V and Plate IX. The heart continues to beat for a short time after respiration has ceased.

THE INFLUENCE OF ROUTE OF ADMINISTRATION.

Decidedly important is the fact that our results show this preparation to be of significant activity when administered orally, as it is employed therapeutically. It is also important that, even when administered orally, the characteristic and significant effects begin almost immediately, or always within five minutes. This fact, together with the persistant character of the action, makes Spirit of Ethyl Nitrite, U. S. P., compare very favorably with the other members of the "nitrite" series.

A COMPARISON OF THE POTENCY OF FRESHLY PREPARED U. S. P. SPIRIT OF ETHYL NITRITE WITH PARTIALLY AND COMPLETELY DETERIORATED SAMPLES, AS INDICATED BY CHEMICAL ASSAY.

By comparing the magnitude and duration of effects upon blood pressure, kidney volume, respiration and urine output, as shown in Plates I, II and III, upon a dog, and Plates VI, VII and VIII, upon a cat, it will be seen that the activity of the freshly prepared sample and the four samples showing varied degrees of deterioration is directly proportional to the ethyl nitrite content as indicated by chemical assay. Deterioration, as indicated by chemical assay, results in the formation of no other pharmacologically active substances of significance in this preparation.

THE SIGNIFICANCE OF p_H.

The p_H of the various preparations studied appears to be of little practical significance as far as influencing the amount of activity is concerned. Generally speaking, the samples showing the highest values in p_H units, showed by chemical assay the lowest ethyl nitrite content and consequently the lowest degree of activity.

SUMMARY.

The quantitative and qualitative pharmacologic activity of freshly prepared and deteriorated samples of U. S. P. Spirit of Ethyl Nitrite of known ethyl nitrite content and p_H has been studied by recording simultaneously the effect upon carotid blood pressure, kidney volume, urine output, respiration and temperature upon anesthetized cats and dogs.

CONCLUSIONS.

1. Spirit of Ethyl Nitrite, U. S. P., has been shown to exert a significant and valuable type of activity when administered by its intended route (orally), by thoroughly reasonable doses.
2. The activity of the preparation diminishes in direct proportion to the loss of ethyl nitrite as determined by chemical assay.
3. The preparation develops no new kind of activity during deterioration which is of any significance when reasonable doses are employed.
4. The general nature of the activity has been shown to be similar to that of the "nitrite" series.

5. Of the effects studied, only those upon circulation and temperature appear to be of therapeutic significance.

6. Our observations do not justify claims of diuretic activity for this preparation.

7. A very safe latitude of therapeutic action has been shown.

8. Lethal doses, intravenously or orally, produce a respiratory death.

9. Since this preparation shows the typical nitrite action, the information provided in authoritative texts regarding methemoglobin production and tolerance development for nitrites as a group, should necessarily be born in mind by the physicians employing this preparation.

10. The p_H values were found to change greatly during deterioration, first showing an early trend toward greater acidity, then changing toward neutrality to a much greater degree. No practical significance is attached to these observations, since it would be impossible to control this factor.

11. Owing to the importance of the high alcohol content relative to the stability of this spirit, prescribing this preparation in any aqueous mixture is to be condemned.

A SUGGESTION.

Since Spirit of Ethyl Nitrite has been shown to possess a therapeutically valuable type of activity, and since it has been definitely established that its lack of stability makes it imperative that it be prepared very near to the time of dispensing, and dispensed in small quantities, we believe that individual small amber-glass ampuls containing the now available ethyl nitrite concentrate, in the amount necessary to make one fluidounce of the spirit, would make it possible to dispense this preparation with its full strength assured.

REFERENCES.

(1) M. J. Andrews, JOUR. A. PH. A., 21 (1932), 799.
(2) M. R. Thompson, *Ibid.*, 20 (1931), 1027.

THE STABILITY OF SOLUTION OF IRON AND AMMONIUM ACETATE U. S. P. X.[1,2]

BY WILLIAM J. HUSA[3] AND GEORGE W. BIRMINGHAM.

INTRODUCTION.

Solution of Iron and Ammonium Acetate, or Basham's Mixture as it is commonly known, though one of the older pharmacopœial preparations, is one which has long been a source of dissatisfaction to physicians and pharmacists. When freshly prepared the solution is a transparent brilliant red liquid and has been referred to as undoubtedly one of the most elegant preparations ever introduced for the administration of iron in dilute solution (1). However, the solution is

[1] Presented before the Scientific Section, A. PH. A., Toronto, Canada, 1932. [2] This paper is based on a thesis presented to the Graduate Council of the University of Florida by George W. Birmingham, in partial fulfilment of the requirments for the degree of Master of Science in Pharmacy.

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prone to rather rapid deterioration, and after standing for a few weeks usually shows considerable turbidity, and frequently very heavy precipitation. For this reason the U. S. P. X directs that this preparation must not be dispensed unless it has been recently prepared.

It has been the purpose of this investigation to study the factors which influence the decomposition of Solution of Iron and Ammonium Acetate, and to seek possible means of retarding the deterioration.

HISTORICAL REVIEW.

1. Development of Formula for Basham's Mixture.—As early as 1831, M. Beral, a French pharmacist, submitted a formula for an "Acétate d'ammoniaque et de fer liquide," or "esprit de mendérérus ferré (2). Toward the middle of the nineteenth century, Dr. William Richard Basham of London recommended a combination of tincture of iron chloride with solution of ammonium acetate and acetic acid as highly beneficial in cases of dropsy, a few drops of the tincture according to the age of the patient being added to a drachm of the Liquor Ammonii Acetatis previously acidulated with acetic acid (3). Apparently Basham's Mixture has never had very wide-spread usage in England and it is not official in the British Pharmacopœia.

The following formula, reprinted from the Pharmacopœia of the Philadelphia Hospital in the *American Journal of Pharmacy* for March 1876, was the first formula given for Basham's Mixture in an American journal: "Liquoris ammonii acetatis *f℥iij*, Tincturæ ferri chloridi *f℥ijss*, Acidi acetici diluti *f℥j*, Curacoa, vel alcohol *f℥ij*, Syrupi, Aquæ āā *q. s. ad f℥vj*." However, a report (4) to the AMERICAN PHARMACEUTICAL ASSOCIATION in 1901 gave the following, from a revised edition of the Pharmacopœia of the Philadelphia Hospital, with the notation that it was believed to have been the original formula of Dr. Basham: "Tincture of ferric chloride 0.6 cc., diluted acetic acid 1.0 cc., solution of ammonium acetate 8.0 cc., elixir of orange 2.0 cc., glycerin 2.0 cc., water, *q. s.* 15.0 cc." In this formula, the quantity of the tincture was slightly reduced and the acetic acid increased. Many variations of the formula were in use in this country prior to the admittance of the solution to the U. S. P. of 1880. J. T. Shinn (5) in 1876 reported at a meeting of the Philadelphia College of Pharmacy that he had found Basham's Mixture prescribed, and that there was a difference in the recipe as obtained from different sources. The statement was made that twenty minims of the tincture and one fluidounce of solution of ammonium acetate were the correct proportions, though no other ingredients of a working formula were given.

The remedy having attained much popularity, and as there was some doubt as to the proper proportion of ingredients, Wiegand (6) in 1887 submitted a formula for Basham's Mixture containing tincture of ferric chloride 3 parts, diluted acetic acid 4 parts, solution of ammonium acetate 32 parts, curacoa 8 parts, syrup of orange peel 12 parts, and water sufficient to make 64 parts. This formula he stated had been given him by a Charles Bullock who he believed had copied it from an English journal (3).

However, a few years later when the solution appeared as official in the U. S. P. of 1880, this formula was changed slightly by the replacement of curacoa and syrup of orange peel by elixir of orange and simple syrup, the change being made, as was suggested by Haussmann (7), because of a deep brown almost black color given to the preparation by the syrup of orange peel. The strength in active ingredients was cut down to almost half what had formerly been recommended, the formula being as follows: "Tincture of chloride of iron 2 parts, diluted acetic acid 3 parts, solution of acetate of ammonium 20 parts, elixir of orange 10 parts, syrup 15 parts, water 50 parts, to make 100 parts."

The title of Basham's Mixture as it was given in the U. S. P. of 1880 was "Mistura Ferri et Ammonii Acetatis." The Dispensatory (1) at that time made the comment that the title was unfortunate in that this was not a mixture from a pharmaceutical point of view, but a transparent bright red liquid in which all the ingredients were in perfect solution, hence it was properly a Liquor. In accordance with this view the 1890 pharmacopœial title was changed to "Liquor Ferri et Ammonii Acetatis." In 1887 the *Druggists Circular* had published a suggestion, made by H. R. LeValley, that the syrup of the official formula be replaced by glycerin, reporting that a solution so made had remained free from precipitation after standing thirty-five days (8). Accordingly, twelve per cent by volume of glycerin was added to the official formula at that time.

At the same time the newly official aromatic elixir replaced the elixir of orange, leading to the following formula: "Tincture of ferric chloride 20 cc., diluted acetic acid 30 cc., solution of ammonium acetate 200 cc., aromatic elixir 100 cc., glycerin 120 cc., water, a sufficient quantity to make 1000 cc."

The first official formulas for Basham's Mixture (those of the U. S. P. of 1880 and 1890) were radical departures from the formulas originally used and upon which the reputation of the preparation was first established, in that the quantities of the active ingredients were cut down about half. Concerning this J. W. England (3) wrote, "In an attempt to secure pharmaceutical elegance and permanency of product, therapeutical efficiency has been sacrificed or largely nullified." Haussmann (7) reported in 1891 that from a medical point of view the slight amount of active ingredients in the official formula was objectionable. For that reason, he said, many physicians prescribed it in extemporaneous solution, while others specified "old formula," referring to a modification printed in the U. S. Dispensatory at that time which was nearly three times the iron strength of the official formula. To meet these objections the U. S. P. of 1900 brought the amounts of tincture of ferric chloride and of solution of ammonium acetate up to four per cent and fifty per cent by volume, respectively, as compared with two and twenty per cent in the earlier official formula. At the same time the volume of aromatic elixir was brought up to twelve per cent, thus making the formula: "Tincture of ferric chloride 40 cc., diluted acetic acid 60 cc., solution of ammonium acetate 500 cc., aromatic elixir 120 cc., glycerin 120 cc., distilled water, a sufficient quantity to make 1000 cc." This formula has not been changed in succeeding revisions up to the present.

In Basham's Mixture ferric acetate in some form—probably a basic acetate as suggested by Weinland (9) (10)—is produced. The presence of ammonium acetate in great excess is a valuable factor therapeutically, since it is held that much of the good achieved from the use of this preparation in kidney disorders depends on the diuretic properties of the ammonium acetate (11). The aromatic elixir is present chiefly as an adjuvant, while the glycerin serves mainly to stabilize the preparation to a certain extent.

2. Chemical Composition and Deterioration of Solutions of Ferric Salts.—The changes which occur in aqueous solutions of ferric salts have long been known and attributed to hydrolysis. The change is progressive, depending on the natural stability of the particular salt, and on such conditions as dilution, temperature, etc. Conditions which increase the hydrolysis of ferric salts at first deepen the color to a clear but intense red, and finally precipitate ferric hydroxide (12). The primary darkening is generally attributed to the formation of colloidal ferric hydroxide, or a highly hydrated oxide (13), after which the particles agglomerate and come down as a heavy precipitate.

The mechanism of the deterioration of solutions of ferric salts has been studied from time to time. Kruke (14) in 1871 believed that the process could be separated into two stages, *first*, a darkening due to formation of soluble ferric oxide (Graham's oxide) and free HCl, and *second*, a turbidity and deposition, according to concentration and temperature, of either difficultly soluble ferric oxide (Pean's), ferric oxychloride or dense anhydrous ferric oxide. Kruke concluded that in solutions of ferric chloride the amount of decomposition increases with rise in temperature and that stability toward heat decreases on dilution. Antony and Gigli (15) after studying the reaction quantitatively concluded that ferric chloride is hydrolyzed in three stages giving $FeCl_2(OH)$, $FeCl(OH)_2$ and $Fe(OH)_3$. Puxeddu (16) in 1923, after certain conductivity and thermochemical measurements, was led to conclude that the changes were even more complex than had heretofore been indicated. In general, however, the solutions of ferric salts do not hydrolyze to the extent of actual precipitation under ordinary conditions of temperature.

Tian (17) explains this on the ground that while the colloidal particles tend to form particles of larger size, an equilibrium is established owing to chemical forces tending to increase dispersity.

All ferric salts in solution undergo the same or a similar type of hydrolytic change as has been shown to be true of ferric chloride, though the hydrolysis is most apparent in the salts of the weaker acids. Thus ferric acetate is one of the most extensively hydrolyzed and consequently one of the least stable of the ferric salts, showing very rapid hydrolysis especially in dilute solutions, even at room temperature. The feebleness of the union of ferric acetate was first pointed out by Pean de St. Gilles (18). It was further shown by Berthelot (19) that a few minutes of boiling effected almost complete disunion of the acid and base followed by a molecular coagulation or condensation after which precipitation occurred.

The dark red color of ferric acetate solutions has generally been attributed to the undissociated molecules (20). Weinland and Gussmann (10), however, state that it has not been found possible to prepare the tri-acetate of iron, and that the red color is due to a mono-acetate of a base, having the formula $[Fe_3(CH_3COO)_6(OH)_2].CH_3COO$. They showed that the precipitate obtained on boiling a solution containing ferric chloride and sodium acetate corresponds approximately with the composition $Fe_3(CH_3COO)(OH)_2O_3$. It would appear that the deep red color is due to the presence of a product of hydrolysis in colloidal suspension, since Hammett (12) explains that the addition of the acetate ion to ferric salt solutions produces the same deep red color as do other methods of increasing hydrolysis. Thus a dialyzed solution of colloidal ferric hydroxide shows approximately the same color as Basham's Mixture.

3. Deterioration of Basham's Mixture.—It can readily be seen that in such a dilute solution of ferric acetate as Basham's Mixture the hydrolysis will be very rapid. Graff (21) in 1894 suggested that the addition of a few drops of 36% acetic acid to the solution of ammonium acetate before adding the excess of acid directed by the U. S. P. would insure much greater stability of the solution. He also suggested that the heat developed in adding the alcoholic tincture of ferric chloride to the aqueous ammonium acetate solution possibly hastens formation of the basic acetate of iron, and that this might be avoided by first diluting the tincture with an equal volume of water and allowing to cool before adding it in its regular order. Haussmann (7) also suggested that increasing the amount of acetic acid was perhaps the only remedy against the instability of the solution. However, a too great excess of acid is objectionable from the standpoint of palatability.

The relation of acidity and alkalinity to the stability of this preparation is of special interest in the light of certain research dealing with the colloidal nature of the "scale preparations" of iron (iron and ammonium citrate, iron and ammonium tartrate, etc.), solutions of which bear marked similarity to Basham's Mixture. Graham (22) in 1862 observed that ferric hydroxide is readily peptized in alkaline solutions of organic hydroxy compounds. Hakomari (23) concluded from certain conductivity, dialysis and ultra-microscopic measurements that the non-precipitability of iron in hydroxy-acid solutions is due partly to formation of a complex between the iron and the hydroxy-acid. Bancroft (24) and Bachman (25), who investigated products from adding sodium hydroxide to iron solutions in presence

of glycerol, sucrose and other non-dissociating hydroxy compounds, concluded that the metal is present partly as a colloid and partly as a crystalloid complex. Morton (26) from results of glass electrode and dialysis measurements observed a definite stability of iron compounds of the "scale salt" type (hydroxy-acid complexes of iron) in alkaline solutions, and concluded that in acid solutions these complexes are present mainly as true electrolytes, but in alkaline solutions they are decomposed to varying extents with the formation of basic hydrosols which are readily peptized and protected by the hydroxy-acid anion. Chatterji and Dhar (27) also showed that ferric hydroxide is peptized by adding sodium hydroxide to solutions of ferric salts in the presence of glycerol or sugar, although these substances will not peptize if added after precipitation has occurred. Todd (28) observed the same thing and reported that samples of iron and ammonium citrate which in aqueous solution are neutral or slightly alkaline remain bright and free from precipitation much longer than do samples which give an acid reaction.

The stability of Basham's Mixture was improved by the replacement of the syrup of the older formula by glycerin, as suggested by LeValley (8). It has been reported (29) that by doubling the amount of glycerin in the official formula, solutions have been prepared which have kept perfectly clear for a period of over eighteen months exposed to ordinary conditions of diffused light. Dunning (30) reported on a formula for Basham's Mixture in which the amount of glycerin was increased from 12 to 20 per cent by volume, which remained without change for more than a year.

Krantz (31) concluded that the superior preserving power of glycerin over an equal weight of sugar in Basham's Mixture is due to the higher molecular concentration of the former, with resulting greater protection against collision and reaction of the hydroxyl ions of water with the ferric acetate molecules.

EXPERIMENTAL PART.

Materials Used.—The U. S. P. X requires that ammonium carbonate shall yield not less than 30% and not more than 32% of NH_3. The samples used in the present investigation were assayed by the U. S. P. method; the NH_3 content ranged between 31.87 and 32.00%. Solution of Ammonium Acetate was made by one of the alternative processes, *i. e.*, by dissolving ammonium carbonate in diluted acetic acid, the latter being adjusted to 6.0%. The strength of Solution of Ferric Chloride was checked by specific gravity determinations. Both the solution and the tincture of ferric chloride were freshly prepared for each experiment, to overcome the difficulty of various degrees of hydrolysis in solutions of different ages.

General Methods.—The solutions were exposed under various conditions, 50-cc. portions in 2-oz. prescription bottles being placed in direct sunlight on the roof, in diffused light at room temperature and in darkness at room temperature. An accelerated aging test was carried out by placing bottles of the various solutions in a constant temperature oven, using temperatures specified in the tables which follow. An aging test of this character was used by Thomas and Hamburger (32) in testing the stability of ferric oxybromide hydrosols.

The solutions on exposure were examined daily, and the time of decomposition recorded was that which elapsed before the formation of a characteristic dense

precipitate. Instances in which only discoloration of the solution, turbidity or precipitation of a special type were found have been specially noted. In all experiments the stability of the modified solution was compared with that of a control which was exactly U. S. P. in every respect and prepared at the same time that the particular experiment was being carried out.

Effect of Colored Bottles.—A test was carried out in which U. S. P. Basham's Mixture in glass bottles of different colors was exposed under various conditions.

TABLE I.—DECOMPOSITION OF BASHAM'S MIXTURE IN VARIOUS COLORED GLASS BOTTLES UNDER VARIOUS CONDITIONS.

Color of Bottle.	Days after Which Precipitation Was Observed. Sunlight.	Diffused Light.	Dark.
Colorless	6	18	20
Green	6	18	20
Brown	14	20	20
Black	23	23	23

Table I indicates that the solution is most stable in black bottles, less stable in amber-colored bottles and least stable in colorless or greenish bottles. In black bottles the stability was uniform under all conditions of exposure tested, while the other bottles offered less protection against the decomposing effect of sunlight.

Effect of Varying Individual Ingredients.—Experiments were carried out to determine the effect of varying the amounts of the individual ingredients one at a time.

TABLE II.—DECOMPOSITION OF BASHAM'S MIXTURE CONTAINING VARIED AMOUNTS OF GLYCERIN (OTHER INGREDIENTS PRESENT IN U. S. P. PERCENTAGE).

Glycerin, %.	Minutes. Oven, 90° C.	Time after Which Precipitation Was Observed. Days. Sunlight.	Diffused Light.	Dark.
0	20	1	1	1
2	40	1	1	1
5	40	1	1	1
8	40	2	4	4
12 (U. S. P.)	50	6	18	21
18	50	8	23	24
24	70	15	*	*

* No precipitation after 103 days.

Table II shows the importance of having at least the U. S. P. proportion of glycerin in the formula and indicates that an increase in the percentage of glycerin gives a more stable solution.

TABLE III.—DECOMPOSITION OF BASHAM'S MIXTURE CONTAINING VARIED AMOUNTS OF ELIXIR (OTHER INGREDIENTS PRESENT IN U. S. P. PERCENTAGE).

Aromatic Elixir, %.	Minutes. Oven, 90° C.	Time after Which Precipitation Was Observed. Days. Sunlight.	Diffused Light.	Dark.
0	50	1	4	4
2	50	4	10	12
5	50	4	10	12
8	50	5	15	18
12 (U. S. P.)	50	6	18	21
18	60	6	25	24
24	40	6	18	23

Stability of the solution increases with the amount of aromatic elixir in the formula up to a certain point, 18 per cent giving the greatest stability.

TABLE IV.—DECOMPOSITION OF BASHAM'S MIXTURE CONTAINING VARIED AMOUNTS OF ACETIC ACID (OTHER INGREDIENTS PRESENT IN U. S. P. PERCENTAGE).

Diluted Acetic Acid, %	Minutes. Oven, 90° C.	Time after Which Precipitation Was Observed. Days. Sunlight.	Diffused Light.	Dark.
0	50	6	78 (Slight)	78 (Slight)
2	50	6	15	16
4	50	6	18	21
6 (U. S. P.)	50	6	18	21
8	35	1*	4*	4*
12	35	1*	4*	4*
18	35	1*	4*	4*

* Light precipitate which redissolved on shaking.

Table IV indicates that the stability of the solution in diffused light and darkness is greatly increased by leaving out the diluted acetic acid.

TABLE V.—DECOMPOSITION OF BASHAM'S MIXTURE CONTAINING VARIED AMOUNTS OF FERRIC CHLORIDE (OTHER INGREDIENTS PRESENT IN U. S. P. PERCENTAGE).

Tincture of Ferric Chloride, %	Minutes. Oven, 75° C.	Time after Which Precipitation Was Observed. Days. Sunlight.	Diffused Light.	Dark.
4 (U. S. P.)	105	6	14	17
8	120	7	16	19
12	120	9	20	22

The stability of the solution increases slightly as the percentage of tincture of ferric chloride increases.

Effect of Various Ingredients in Absence of Others.—To further determine the effect that the individual ingredients have upon the stability of the solution, samples were prepared in which only the quantities of the tincture of ferric chloride and solution of ammonium acetate were kept at the U. S. P. percentage. In this

TABLE VI.—DECOMPOSITION OF BASHAM'S MIXTURE CONTAINING VARIED AMOUNTS OF SOLUTION OF AMMONIUM ACETATE (DILUTED ACETIC ACID, AROMATIC ELIXIR AND GLYCERIN OMITTED).

Solution of Ammonium Acetate, %	Minutes. Oven, 75° C.	Time after Which Precipitation Was Observed. Days. Sunlight.	Diffused Light.	Dark.
0	*	*	*	*
2	*	*	*	*
4	*	*	*	*
6	*	*	*	*
10	*	*	*	*
25	45	1	1	1
40	45	1	1	1
50	45	1	1	1
60	30	1	1	1
70	30	1	1	1
80	30	1	1	1
Control (U. S. P. formula)	70	6	15	18

* No precipitation after 81 days.

way the effect of the different ingredients independent of the presence of other substances was tested by varying the percentages in the aqueous ferric acetate solutions. A preliminary experiment was run by varying the proportions of solution of ammonium acetate added to the U. S. P. quantity of tincture of ferric chloride.

In absence of stabilizing ingredients, 10% of solution of ammonium acetate does not cause precipitation but 25% or more causes precipitation.

TABLE VII.—DECOMPOSITION OF BASHAM'S MIXTURE CONTAINING VARIED AMOUNTS OF DILUTED ACETIC ACID (AROMATIC ELIXIR AND GLYCERIN OMITTED).

Diluted Acetic Acid, %	Minutes. Oven, 75° C.	Time after Which Precipitation Was Observed. Days. Sunlight.	Diffused Light.	Dark.
0	40	1	1	1
2	40	2	1	1
4	40	2	1	1
6	40	2	2	2
10	40	2	2	3
25	70	3	7	9
Control (U. S. P. formula)	100	6	22	29

In absence of aromatic elixir and glycerin the stability increases with increasing percentage of diluted acetic acid, but even with 25% of diluted acetic acid the solution is much less stable than the U. S. P. formula.

TABLE VIII.—DECOMPOSITION OF BASHAM'S MIXTURE CONTAINING VARIED AMOUNTS OF AROMATIC ELIXIP (DILUTED ACETIC ACID AND GLYCERIN OMITTED).

Aromatic Elixir, %	Minutes. Oven, 75° C.	Time after Which Precipitation Was Observed. Days. Sunlight.	Diffused Light.	Dark.
0	45	1	1	1
2	45	1	1	1
4	45	1	1	1
6	45	1	1	1
10	45	1	1	1
25	55	1	3	3
40	55	1	7	10
Control (U. S. P. formula)	70	6	15	18

In absence of glycerin and diluted acetic acid, solutions of even a high percentage of aromatic elixir are not as stable as the U. S. P. formula.

TABLE IX.—DECOMPOSITION OF BASHAM'S MIXTURE CONTAINING VARIED AMOUNTS OF GLYCERIN (DILUTED ACETIC ACID AND AROMATIC ELIXIR OMITTED).

Glycerin, %	Minutes. Oven, 75° C.	Time after Which Precipitation Was Observed. Days. Sunlight.	Diffused Light.	Dark.
0	30	1	1	1
2	30	1	3	3
4	55	1	7	10
6	60	2	12	15
10	60	4	27	29
25	180	11	*	*
40	360	27	*	*
Control (U. S. P. formula)	75	6	15	18

* No precipitation after 81 days.

In absence of diluted acetic acid and aromatic elixir, the solution with 10% glycerin (less than U. S. P.) is more stable in diffused light and darkness than the solution of the U. S. P. formula; stability increases with the amount of glycerin.

Effect of Addition of Alkali.—Tests were made in which diluted acetic acid was omitted and small amounts of NaOH added at a point following the mixing of the solution of ammonium acetate and tincture of ferric chloride. Under ordinary conditions of storage these were more stable than the U. S. P. formula. Likewise the addition of sodium acetate appeared to increase the stability. Since the greater stability of the less acid solutions under ordinary conditions seemingly refutes the long prevalent idea that slight increases in the acidity of Basham's Mixture improve the stability, further work is in progress on this point.

Effect of Sucrose.—The effect of sucrose on the stability of the solution was tested in one series of experiments in which varying percentages were added to solutions made U. S. P. in respect to ferric chloride and ammonium acetate content, the other ingredients of the U. S. P. formula being omitted. Another series of tests was made in which the sugar was added to the regular U. S. P. formula. In both cases the sugar was added to the solution of ammonium acetate before the tincture of ferric chloride was added, and as much of it as possible put into solution before making the other additions.

TABLE X.—DECOMPOSITION OF BASHAM'S MIXTURE CONTAINING VARIED AMOUNTS OF SUCROSE (DILUTED ACETIC ACID, AROMATIC ELIXIR AND GLYCERIN OMITTED).

Sucrose, %	Time after Which Precipitation Was Observed. Minutes. Oven, 75° C.	Days. Sunlight.	Diffused Light.	Dark.
0	45	1	1	2
2	45	1	1	2
4	45	1	2	2
6	45	1	2	3
10	45	1	3	3
25	60	2	3	3
40	60	4	4	4
Control (U. S. P. formula)	75	6	15	18

Table XI indicates that sucrose alone is not effective in stabilizing the solution.

TABLE XI.—DECOMPOSITION OF BASHAM'S MIXTURE CONTAINING VARIED AMOUNTS OF SUCROSE (FORMULA CONFORMS TO U. S. P. IN OTHER RESPECTS).

Sucrose Added, %	Time after Which Precipitation Was Observed. Days. Sunlight.	Diffused Light.
0 (U. S. P.)	6	12
2	7	13
4	7	19
6	7	*
10	8	*
25	10	*
40	20	*
50	33 (slight)	*
60	33 (slight)	*
65	33 (slight)	*

* No precipitation in 42 days.

These experiments suggest that it would be well to consider an increase in the percentage of sucrose in the official formula, *i. e.*, adding some in addition to that present in the aromatic elixir. It is apparent that Basham's Mixture might be prepared in the form of a syrup, which would be more stable and possibly more palatable than the solution. It is interesting to note that a formula for a syrup of this kind was presented many years ago by M. Beral (2), who called his preparation "sirop d'acétate d'ammoniaque et de fer."

Effect of Other Additions.—From the tests carried out thus far it appears that the following tentative conclusions may be drawn. HCl in high concentration retards precipitation, though low concentrations hasten the appearance of a light precipitate. Large quantities of NaCl hasten decomposition, but smaller amounts appear to have a stabilizing effect. NH_4Cl increases the stability in diffused light and darkness. Rochelle salt and sodium citrate have a marked stabilizing influence; the higher percentages of these salts caused discoloration in the solutions stored in sunlight. Protective colloids such as gelatin, agar, acacia and tragacanth were not effective as stabilizers in Basham's Mixture in absence of glycerin, diluted acetic acid and aromatic elixir; when used in addition to the ingredients of the U. S. P. formula there was some increase in stability in the following concentrations: gelatin 1%, agar 0.2%, acacia 1%.

Stability toward Electrolytes.—The stability of colloidal solutions is sometimes considered from the standpoint of precipitation by electrolytes. Since an examination of the tables indicates that the results in the accelerated heat test are not directly proportional to the stability under usual conditions, some attention was devoted to the question of whether the stability of Basham's Mixture toward electrolytes would bear a definite relation to stability under usual conditions of storage. Tests were carried out to determine the minimal precipitating concentrations of Na_2SO_4 and of Na_2HPO_4 for official Basham's Mixture and some of the modified formulas.

TABLE XII.—DECOMPOSITION OF BASHAM'S MIXTURE OF VARIOUS FORMULAS COMPARED WITH STABILITY TOWARD ELECTROLYTES.

Composition.	Time for Precipitation. Minutes. Oven, 75° C.	Days. Sunlight.	Days. Diffused Light.	Dark.	Minimal Precipitating Concn. in Millimoles. Na_2SO_4.	Na_2HPO_4.
U. S. P.	75	6	15	18	7.5	0.04
U. S. P. (dil. acetic acid, glycerin and elixir omitted)	45	1	1	1	4.5	0.005
U. S. P. (dil. acetic acid omitted)	80	6	62	*	5.0	0.035
U. S. P. plus 1% *N* NaOH	80	6	74	*	5.0	0.030
U. S. P. plus 24% glycerin	180	15	*	*	8.5	0.045

* No precipitation in 90 days.

From the results in Table XII, it appears that the accelerated heat test gives a better indication of the stability under ordinary conditions than does the precipitation test with electrolytes.

SUMMARY.

1. The decomposition of Basham's Mixture is accelerated by light and heat.

2. It is important to have at least the U. S. P. proportion of glycerin in the formula and an increase in the percentage of glycerin gives a more stable solution.

3. Stability of the solution increases with the amount of aromatic elixir in the formula up to a certain point, 18% giving the greatest stability.

4. Under ordinary conditions of storage Basham's Mixture appears to be more stable when the diluted acetic acid is omitted, with or without the addition of small quantities of NaOH or sodium acetate. Further work is in progress on this point.

5. Sucrose in high percentages is an effective stabilizer if used in presence of all the ingredients of the official formula.

6. The stability of the solution is increased slightly by increasing the quantity of tincture of ferric chloride used.

7. The stability of the solution is increased by HCl, NH_4Cl and by small quantities of NaCl, but high concentrations of NaCl hasten precipitation.

8. Rochelle salt and sodium citrate increase the stability of the solution.

9. Certain proportions of gelatin, agar and acacia increase the stability somewhat when used in addition to the ingredients of the U. S. P. formula.

10. An accelerated heat test gives a better indication of the stability under ordinary conditions than does a precipitation test with electrolytes.

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BROM DERIVATIVES OF HYDROTHYMOQUINONE.*

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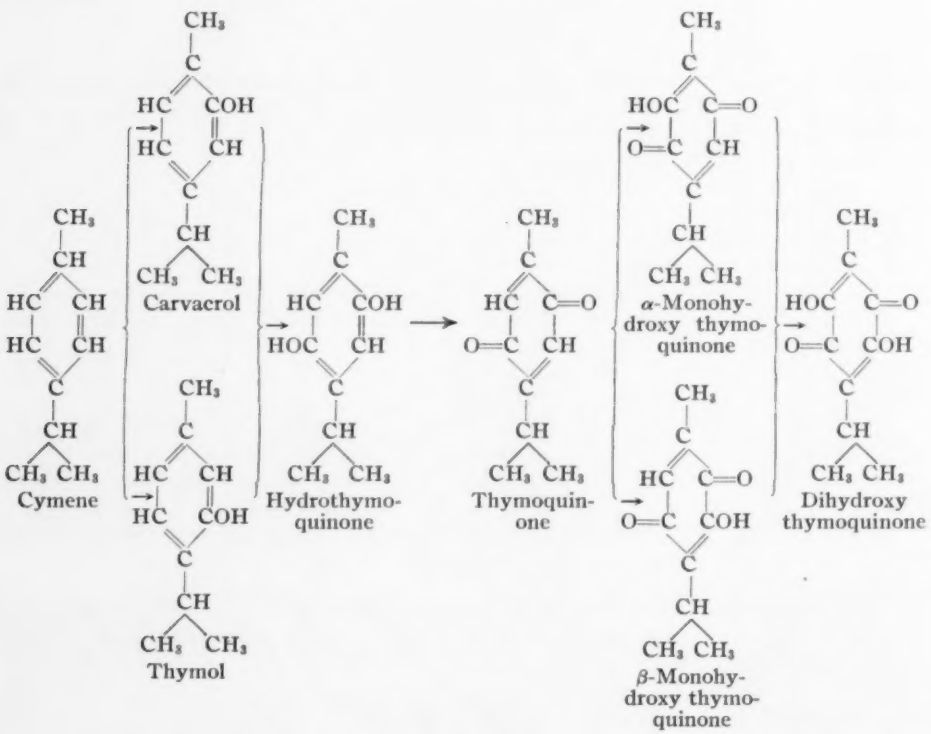
In the course of a bactericidal study of oxygenated derivatives of cymene, a striking group has been studied in connection with the phytochemical investigation of various species of the genus Monarda. The chemical relationship of its members can readily be understood by a glance at the following structural formulas:



It has been noted that to a certain extent an increase in the hydroxyl content resulted in a corresponding elevation of bactericidal potency (1). In other words,

* Scientific Section, A. Ph. A., Toronto meeting, 1932.

the phenol coefficients of hydrothymoquinone were found to be higher than those of either of the monatomic phenols. With this in mind, a more thorough study of the derivatives of hydrothymoquinone next suggested itself. Interest was directed more particularly to the halogen derivatives, especially in the light of the fact that the chloro and bromo compounds of both thymol and carvacrol showed unusual bactericidal efficiency.

The bromine containing compounds will be discussed first. On a previous occasion, the writer had made a preliminary study of the direct bromination of hydrothymoquinone and it was observed that oxidation was brought about with the resulting formation of bromine substitution products of thymoquinone. By the direct bromination of hydrothymoquinone with one, two, three and four moles of bromine, respectively, in acetic acid solution, the products which were obtained are compared below with the corresponding brom derivatives of thymoquinone:

1. The action of Br_2 resulted in the formation of 6-monobromthymoquinone (2) which crystallized in yellow needles that melted at 48° and that were soluble in alcohol, chloroform and benzene.

2. The action of 2 Br_2 resulted in the formation of 3,6-dibromthymoquinone (3) which crystallized in yellow needles that melted at 73° and were insoluble in cold alcohol, but soluble in hot alcohol, in cold ether, chloroform and acetone.

3. The action of 3 Br_2 resulted in the formation of the same tribromide (4) that had previously been obtained from thymoquinone, which crystallized in yellow laminæ that melted at 65°, and were insoluble in cold alcohol, but soluble in hot alcohol, also in ether and acetone.

4. Whereas the action of 4 Br_2 on thymoquinone had resulted in the formation of a monobromide (5) melting at 53° and of the 3,6-dibromide melting at 73°; the action on hydrothymoquinone gave the same yellow laminæ of the tribromide melting at 65° (see No. 3).

It becomes evident, therefore, that the preparation of the bromhydrothymoquinones will have to be brought about by some other method. A study of the literature reveals that the first mention of the mono- and dibromhydrothymoquinone was made by Schniter (2) and Schulz (6) in 1882, however, not as such but as the respective acetates. They prepared the 6-monobromhydrothymoquinone diacetate by treating thymoquinone with acetylbromide. In 1887, Schniter (7) effected the formation of 6-monobromhydrothymoquinone by the action of HBr on thymoquinone. However, he reported its melting point as 53°, whereas the melting point of 63–64° has been obtained in this investigation.

6-Monobromhydrothymoquinone.—(*a*) *Reduction with Sulphur Dioxide.*—The 6-monobromthymoquinone was prepared by the bromination of thymoquinone in chloroform solution at 5°, whereby yellow needles were obtained, which when recrystallized from 95 p. c. alcohol, melted at 48–49°. It has been observed that by treating 10-Gm. portions of thymoquinone with a mono-molecular equivalent (14.7 Gm.) of bromine, the mono compound only is formed. Larger quantities yield chiefly the dibromthymoquinone, m. p. 73° with low yields of the monobrom derivative.

5 Gm. of 6-monobrom thymoquinone were dissolved in a 75 p. c. alcohol. This solution was then saturated with SO_2 gas, the reaction mixture being kept at a temperature of from 40–50°. The solution was then allowed to evaporate

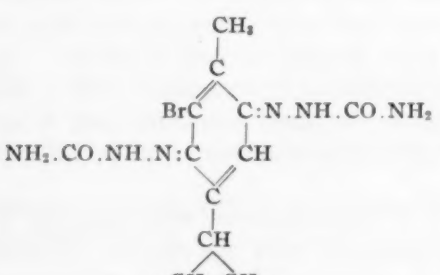
spontaneously, whereby the 6-monobromhydrothymoquinone formed as light orange plates in almost theoretical yield. These were thoroughly dried by pressing on a porous plate and were found to melt sharply at 63–64°. For further purification, this substance was gently boiled in alcoholic solution with one Gm. of Darco, a commercial activated charcoal. The filtrate yielded the same light orange plates, m. p. 63–64°. A bromine determination by the Carius method yielded 32.6 p. c., the theoretical bromine content being 32.6 p. c.

When acetylated with sodium acetate and acetic acid anhydride, white prisms, m. p. 91° (6), of the monobrom diacetate were formed.

(*b*) *Reduction with Zn and HCl.*—5 Gm. of 6-bromthymoquinone were suspended in 95 p. c. alcohol to which 20 cc. of concd. HCl had been added. To this was added zinc dust in portions of about 0.2 Gm. while the mixture was refluxed until all of the solid had been completely dissolved. The mixture was then refluxed for an additional half hour, the solution filtered through a hot water funnel, and the filtrate allowed to cool and evaporate spontaneously. A crop of white crystals was collected, which was recrystallized from hot water, and dried. 2.7 Gm. of hydrothymoquinone, m. p. 140–142°, were obtained. The zinc had evidently extracted considerable of the bromine. A dark brown solid separated out of the mother liquor, which probably was a mixture of 6-monobromthymoquinone, and a quinhydrone formed from unreacted 6-monobromthymoquinone and the hydrothymoquinone. This impure product melted between 85–110° and was readily soluble in alcohol, ether and acetone.

5 Gm. of dibromthymoquinone were then treated as described above, 2.9 Gm. of orange sheaths of the 6-monobromhydrothymoquinone, m. p. 62–64°, were first collected. The mother liquor yielded less than a gram of unreacted dibromthymoquinone, m. p. 73°. The crystal sheaths showed no change in melting point, when recrystallized from hot heptane. The diacetate melted at 91° indicating that a bromine atom had been abstracted.

Mention is also made here of the formation of 6-monobromhydrothymoquinone in an entirely different manner. The writer was studying the feasibility of separating a mixture of mono- and dibromthymoquinone by their respective monosemicarbazides. In doing so 5 Gm. of the above mixture were reacted with an approximate monomolecular equivalent of semicarbazide hydrochloride in 95 p. c. alcohol solution, the contents being refluxed for an hour. On cooling, 1.2 Gm. of a yellow crystalline material were collected by filtration, which melted sharply at 223° and which was identified as the 6-brom dicarbazide of thymoquinone, having the following configuration:



The mother liquor on further concentration yielded 3.6 Gm. of a light orange crystalline deposit, which when recrystallized from hot heptane melted at 62–64°. This substance was further established as 6-bromhydrothymoquinone by its diacetate, m. p. 91°.

Inasmuch as the reducing property of phenyl hydrazine can readily be explained by its liberation of hydrogen according to the equation

$$C_6H_5NH.NH_2 \longrightarrow C_6H_6 + N_2 + H_2 \quad (8)$$

the probability of semicarbazide acting as a reducing agent is not too far fetched. The reaction can possibly be explained in the following manner:

$$2\ H_2N.NHCONH_2 \longrightarrow 2\ NH_2CONH_2 + N_2 + H_2$$

3,6-Dibromhydrothymoquinone.—The literature does not describe this compound as such. Schulz (9), in 1882, prepared its diacetate, by brominating 6-brom diacetate of hydrothymoquinone in ether solution. He assigned to it a melting point of 121–122°, in contrast to 96–97° reported later on in this investigation.

(*a*) *Reduction with Zinc and HCl.* As has been previously described, when dibromthymoquinone was reduced with zinc and HCl, one bromine atom was abstracted to yield the 6-monobromhydrothymoquinone. In the light of these results, tribromthymoquinone was similarily treated to result in the formation of orange rhombic crystals, m. p. 60°. To make use of a mixture of dibrom and tribromthymoquinone, made available in the course of brominations of thymoquinone, the following products were identified from its reduction with zinc and HCl:

Orange rhombic plates, m. p. 59–60°. (Dibromhydrothymoquinone.)
Yellowish orange plates, m. p. 62–64°. (6-Bromhydrothymoquinone.)
Reddish prisms, m. p. 48–50°. (6-Bromthymoquinone.)

Dibromhydrothymoquinone is very readily soluble in alcohol, ether, acetone and heptane, whereas dibromthymoquinone is difficultly soluble in cold alcohol but readily so in hot alcohol, cold ether, acetone and heptane.

Bromine determinations (Carius) revealed as follows:

Found 48.7 p. c., calculated 49.3 p. c.

The diacetate, $C_{10}H_{10}Br_2(OCOCH_3)_2$, was obtained as white prisms when recrystallized from hot absolute alcohol, m. p. 96–97°. Schulz reported a melting point of 121–122° for this same substance, preparing it, however, by brominating the 6-bromdiacetate of hydrothymoquinone. When analyzed for bromine, the compound, m. p. 96–97°, contained 38.5 p. c.; calculated for $C_{10}H_{10}Br_2(OCOCH_3)_2$, 39.2 p. c.

(*b*) *Reduction with Sulphur Dioxide.* The dibromthymoquinone was then reduced by passing SO_2 into a hot alcoholic solution of the former. On cooling a fraction of a Gm. of the above material, m. p. 73°, was separated by filtration. The filtrate was allowed to concentrate spontaneously, whereupon handsome orange plates were obtained in almost quantitative yield. These were further purified by recrystallization from heptane, melting sharply at 60°.

(*c*) *Reduction with Hydrogen Sulphide.* By treating dibromthymoquinone with an ammoniacal solution of H_2S, a small crop of yellow crystals, m. p. 118–119° was formed, which as yet have not been investigated any further.

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WISCONSIN PHARMACEUTICAL EXPERIMENT STATION.

THE UNSAPONIFIABLE FRACTION FROM SPINACH FAT. II.

BY FREDERICK W. HEYL AND DONALD LARSEN.

In a previous publication (1) from this laboratory, the isolation of a hydrocarbon melting at 67.5–68.5° and two alcohols melting at 76–77° and 87–88°, respectively, was described. The second of these alcohols, of which we obtained but 0.2 Gm., appeared to be a glycol.

In recent papers (2) (3) it has been shown that the hydrocarbon is $C_{31}H_{64}$, hentriacontane.

The point was brought up by the English workers concerning the identity of the alcohol melting at 76–77° with ceryl alcohol (C, 81.67; H, 14.13) with which conclusion our previously reported results are at variance (C, 80.9; H, 14.2). The spinach which we extracted presents a highly complex mixture. It contained not only a preponderant amount of hentriacontane but also a glycol and the last substance appears to be absent from English spinach. The glycol for which we previously reported a m. p. of 87–88° has now been obtained purer and melts at 103.5°.

Elaborate effort has been made to definitely describe the monohydric alcohol and to identify it with certainty. This problem is greatly facilitated by the recent work of Pollard, Chibnall and Piper (4) who isolated pure *n*-hexacosanol from cocksfoot grass (Dactylis Glomerata). They reported that the alcohol melts at 79.7° and its acetate at 59.5–59.6°. Collison and Smedley-Maclean found for their ceryl alcohol from spinach 77–78° and for the acetate 61.5°.

Our further work shows conclusively that the spinach alcohols are a mixture of *n*-tetracosanol and *n*-hexacosanol with the former predominating. It is also shown that fractionation of the paraffin alcohols or of their acetates does not give the satisfactory analysis of this fraction which results finally from working with the corresponding acid mixtures.

Incidentally a new dextro-rotatory sterol has been isolated from the mother liquors of the less soluble spinasterol.

EXPERIMENTAL.

The unsaponifiable material was crystallized from large volumes of 95 per cent alcohol (50 Gm. in 2.5 liters) and the crystals were filtered off after a few hours' standing. These were worked up as reported in the work on spinasterol (5).

The combined filtrates were fractionated and the more insoluble fractions, below this sterol, were digested with relatively small amounts of ether, whereupon an insoluble glycol melting at 103.5° was isolated. (The probable formula is $C_{26}H_{54}O_2$.)

Our work concerns the soluble material in the filtrate. The ether was removed and a prolonged fractionation from methyl alcohol gave a top fraction weighing 5.0 Gm. which was largely hydrocarbon (m. p., 67–72°). Successive crops below this melted, respectively, 70–80°; 65–105°; 70–120°; 65–110°, and a final filtrate (A).

While this work was in progress, we also carried out work upon the alcohol-insoluble material designated (*a*) in our first paper (1). We crystallized this material from alcohol and obtained a top fraction of hydrocarbon and then we repeatedly recrystallized the more soluble material from ether. The melting point of the purified material rises slowly from 73° to 76–77°. Other solvents such as ligroin, chloroform, acetone or methyl alcohol yield no purer crystalline material. This substance corresponds exactly with that previously described. Acetylation gives an acetate melting at 58–59°. The acetate of this fraction obtained by Collison and Smedley-Maclean (3) melted at 61.5°.

Analysis gave figures checking very closely for $C_{22}H_{45}O.CO.CH_3$. (Calc., C, 78.17; H, 13.13. Found, C, 78.13; H, 12.9.) However, when saponified a mean molecular weight of 432 was obtained (calc., 368). The free alcohol recovered after saponification was converted into the acid phthalate by the method of Power (6). Recrystallized four times the acid phthalate melted at 80–81°. The alcohol recovered upon saponification melted at 78–79°. The corresponding acetate melted at 59.5–60.5°. (C, 80.1; H, 13.4.)

It appears that a more systematic study of this mixture is necessary as traces of hydrocarbon and other possible contaminants cause a continued lack of agreement between the percentages of C and H found and the expected mean molecular weight.

We, therefore, took the filtrate (*A*) and the corresponding filtrate from the work on the acetate just described and precipitated the soluble sterol with digitonin. In the case of the preparation of the acetate melting at 58–59°, repeated recrystallizations from ether remove this sterol from the top fractions.

After filtering the insoluble digitonide, the excess of digitonin was removed from the filtrate which was thereupon evaporated to dryness. The residue was separated into (*a*) the alcohol fraction and (*b*) the hydrocarbon fraction by means of the phthalic acid fusion method.

The Dextro-rotatory Sterol.—The sterol fraction was liberated from the digitonide by xylene and then fractionated from absolute alcohol. Less soluble spinasterol rich fractions were discarded and the more soluble fractions consisting largely of the new dextro-rotatory sterol gave 7 successive crops. $(\alpha)_{5461}$ + 5.77° to 6.7°. M. p., 143–149°. Further purification could not be accomplished by this process

and the material was acetylated and the acetate exhaustively and systematically crystallized from ether and alcohol and a further quantity of spinasterol rich sterol separated as acetate $(\alpha)_{5461} = -1.16°$. From the filtrates, after the exclusion of several intermediate crops, acetates were isolated in a series showing $(\alpha)_{5461} = +6.3°$ to 6.8°.

The purest material melted at 150–154° and $(\alpha)_{5461} = +7.2°$.

$C_{29}H_{48}O_2$. Calcd., C, 81.24; H, 11.29
Found, C, 81.23; H, 11.46.

The acetate was saponified by boiling for 15 minutes with 3 per cent alcoholic potash whereupon the sterol separated in plates. Recrystallized from alcohol + ether, it melted at 145–148° and $(\alpha)_{5461} = 7.65°$. No insoluble bromide could be prepared.

The Liebermann-Burchard and Salkowski color tests were positive; the trichloroacetate test of Rosenheim was negative.

The sterol acetate on quantitative reduction in acetic acid solution with platinum oxide as a catalyst absorbed hydrogen approximately for one double bond. The reduced sterol acetate after crystallization from acetic acid gave flat plates melting at 112–113°. A mixed melting point with spinastanol acetate, prepared by the catalytic reduction of spinasterol acetate, was not lowered. β-spinasterol, the more soluble sterol from spinach, is therefore closely related to spinasterol giving the same spinastanol on catalytic reduction.

The fraction consisting of paraffin alcohols was acetylated and the acetates were extensively fractionated from large volumes of absolute alcohol and collected in six fractions: 1, m. p., 62.5–64°; 2, 61.5–63.5°; 3, 60–62°; 4, 58–60°; 5, 56.5–58.5°; 6, 52.5–55°. The molecular weights found upon saponification varied from 467 to 397, but since all fractions were amorphous no more reliable interpretation was possible here than in the case of the acetate previously described.

The alcohols recovered upon saponification from the above six fractions were studied with the following results:

TABLE I.—THE ALCOHOL FRACTIONS.

Fraction No.	Weight.	M. p.	M. p.*		C.	H.
1	0.025	79–81	....		81.98	14.22
2	0.26	75–79	79.5–81		81.75	14.37
3	0.82	79.81	80–81		81.57	14.03
4	0.73	76–79	77–78		81.12	14.07
5	2.12	75–78	76–77		80.89	13.95
6	0.20	77–79	78–79		80.58	13.97
				Calc. $C_{30}H_{62}O$	82.10	14.25
				$C_{28}H_{58}O$	81.86	14.24
				$C_{26}H_{54}O$	81.58	14.23
				$C_{24}H_{50}O$	81.26	14.22
				$C_{22}H_{46}O$	80.89	14.21

* The melting points in the first column are those found after once recrystallizing from alcohol; the second column represents the material after a number of further crystallizations from ether; Fraction 3, after 3; Fraction 5, after 5 more crystallizations.

Since the work on the alcohols agreed in every respect with our work on the acetates, a conclusion might be justified that we had here a complicated mixture of

a series of alcohols including C_{20} to C_{22} members. But the results of oxidation did not bear this out.

Each fraction was now oxidized by the method of Gascard (7).

Fraction 2 gave a product which upon crystallization from alcohol had a m. p. of 82–83°. C, 78.56; H, 13.5. It was recrystallized from alcohol twice, alcohol and ether twice, acetone twice and again from alcohol and ether. M. p., 83–83.5°. C, 78.3; H, 13.24.

Calc. for $C_{26}H_{52}O_2$. C, 78.71; H, 13.22.
$C_{24}H_{48}O_2$. C, 78.17; H, 13.13.

Fraction 3 which was a highly crystalline alcohol gave an acid, m. p., 83–85°. C, 78.58; H, 13.05. Recrystallized eleven times, m. p., 87–87.5°. C, 78.68; H, 13.12. This is pure hexacosanic acid and the corresponding alcohol is pure *n*-hexacosanol. Pollard, Chibnall and Piper (4) found the melting point of the pure acid 87.7–87.9° and for the *n*-hexacosanol 79.7°; for the acetate 59.5–59.6°.

Fraction 4 gave an acid which upon one crystallization had a m. p. of 78–80°. C, 78.14; H, 13.23. Recrystallized eight times from alcohol and ether, m. p., 81–82°. C, 78.53; H, 13.51. This is a mixture of the C_{24} and C_{26} acids.

Fraction 5 which is a crystalline alcohol when oxidized gave an acid, m. p., 80–82°. C, 78.22; H, 12.87. Recrystallized from alcohol and from alcohol + ether mixtures nine times, it had a m. p. of 82.5–83°. C, 78.14; H, 12.7. This acid is pure tetracosanic acid. It should be noted that *n*-tetracosanol is the predominant spinach alcohol.

SUMMARY.

1. In addition to spinasterol, spinach contains a second sterol, $C_{27}H_{46}O$, m. p., 145–148°, and $(\alpha)_{5461} = +7.65°$. The corresponding acetate, m. p., 150–154° and $(\alpha)_{5461} = +7.2°$.

2. The predominant paraffin alcohol is *n*-tetracosanol. *N*-tetracosanic acid melts at 82.5–83°.

3. *N*-hexacosanol was identified and the constants reported for *n*-hexacosanic acid by Pollard, Chibnall and Piper and confirmed.

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"If a druggist was to tell all the trouble and worries that are poured into his ears the story would make an Arabian Nights' tale. And yet you always expect, and you generally find the druggist ready to greet you with a smile. In a very genuine sense the druggist is a friend of all the world. He is not merely a dispenser but he is indispensable."—It is a pleasure to pay this tribute to the druggists of Long Beach.—*The Long Beach* (Calif.) *Sun*—through *Rocky Mountain Druggist.*

A STUDY OF THE ALKALOIDS OF DATURA INNOXIA, MILLER.*

BY EARL E. HESTER[1] AND EDWARD D. DAVY.

A review of the literature revealed that much confusion existed between *D. innoxia* classified and named by Miller in 1768 as recorded in the Eighth Edition of his "Gardener's Dictionary" and that of other *Daturas*. This confusion continued until comparatively recent date as shown by the reviews of Safford[2] and Timmerman.[3]

Datura innoxia, Miller at The Squire Valleevue.

The review, however, revealed nothing with reference to any chemical work having been done upon *Datura innoxia*, Miller, to which this paper is devoted.

The drug used in this work was grown in The Medicinal Plant Garden at The Squire Valleevue. The type of soil is a clay loam, but according to Francis H. Carr,[4] the composition of the soil, fertilizer and seasonal conditions have very little effect upon the alkaloidal content of belladonna, a closely related drug. It was grown and harvested under the direction of Dr. F. J. Bacon. The seeds

* Scientific Section, A. PH. A., Toronto meeting, 1932.

[1] Submitted in partial fulfilment of the requirements for the degree of Master of Science at Western Reserve University.

[2] William E. Safford, *Annual Reports of The Smithsonian Institute*, 1920, pages 537–567.

[3] Helen A. Timmerman, *Pharmaceutical Journal and Pharmacist*, 118 (1927), 571.

[4] Francis H. Carr, *American Journal of Pharmacy*, 85 (1913), 487–496.

from which this plant was grown were supplied by Dr. A. F. Sievers of The Bureau of Drug Plant Industry, Washington, D. C.

The leaves were carefully selected and separated from the stems by hand and then milled. The ground leaves were passed through a Number 20 sieve. This size powder was used throughout in the assay, the report of which follows.

In the assays which follow on *D. innoxia*, Mill. the total yield was based upon the molecular weight of atropine which is the practice in Pharmacopœial standardizations for the mydriatic drugs.

Opinions differ greatly as to the proper solvent and other conditions involved in the assay of mydriatic drugs. An effort was made to learn why such discrepancies should occur when obviously it was not a question of the analyst. This led to the use of the following solvents and conditions modifying the conventional method.

GENERAL METHODS.

The U. S. P. X Method of Assay for Strammonium.

Results.

(1) 0.402% (2) 0.394% (3) 0.426%

Modifications of U. S. P. X Method.—A. The final chloroformic extract was evaporated on a water-bath to approximately 5 cc.; standard acid was added, and the remaining chloroform dissipated at water-bath temperature.[1]

Results.

(1) 0.574% (2) 0.509% (3) 0.520%

B. Standard Acid was added to final chloroform extract before any reduction in volume.

Results.

(1) 0.549% (2) 0.567%

C. Drug exhausted until negative to *p*-dimethylamino-benzaldehyde solution.[2] Standard acid added to last 5 cc. of final chloroformic extract.

Result.

0.557%

D. Solvent:

Alcohol	10 cc.
NH_4OH (28%)	5 cc.
Ether	20 cc.

After the addition of the initial solvent in which the drug was macerated, ether was used to exhaust the drug.

1. The final chloroformic extract was allowed to evaporate spontaneously, then permitted to stand three days in a covered beaker after all the chloroform had evaporated.

Results.

(1) 0.438% (2) 0.448%

2. The final chloroformic extract was evaporated on a water-bath to approximately 5 cc.; standard acid was added, and the remaining chloroform evaporated at water-bath temperature.

Results.

(1) 0.542% (2) 0.546%

[1] Suggested by Watkins and Palkin.

[2] YEAR BOOK OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 4 (1915), 340.

3. Drug exhausted until negative to *p*-dimethylamino-benzaldehyde. Standard acid added to last 5 cc. of final chloroformic extract.

Result.
0.661%

E. Solvent. Chloroform used as the solvent throughout.

1. The final chloroform extract was allowed to evaporate to dryness spontaneously.

Result.
0.417%

2. Standard acid was added to the last 5 cc. of final chloroformic extract, after which the chloroform was evaporated from a water-bath.

Results.
(1) 0.450% (2) 0.461%

3. Drug exhausted until negative to *p*-dimethylamino-benzaldehyde. Standard acid added to last 5 cc. of final chloroformic extract.

Result.
0.713%

The objection to chloroform as a solvent is the tendency toward the formation of air pockets and channeling thereby preventing the chloroform from exerting its maximum solvent action within a limited time.

Upon comparing the results obtained, the differences prompted additional analyses in an attempt to interpret these variations.

F. U. S. P. X solvent for extraction of drug. In the assay of another portion of drug, the final chloroform extract was washed well with water to remove any ammonia that might be present and then passed through absorbent cotton. The chloroform extract was then evaporated on a water-bath to 10 cc. (a measure to insure the complete dissipation of any free ammonia). The flask containing the concentrated chloroform extract was then connected in a manner that "washed air" (air washed successively with dilute H_2SO_4 and caustic soda solution) was drawn through the flask, heated on a water-bath and the vapors passed into standard acid (5 cc.) (0.02 *N* H_2SO_4). After the residue in the flask had been reduced to dryness the heat and passage of washed air over the alkaloidal residue were continued ten minutes longer.

The flask containing the standard acid was then heated on a water-bath to volatilize the chloroform. It was cooled to room temperature and diluted to exactly 50 cc. Ten cubic centimeters were then nesslerized. A brown precipitate formed immediately. The remainder upon titration and calculating the total volatile material as alkaloid showed 0.0847%.

The alkaloidal residue remaining in the flask was titrated with the following result: 0.3743%.

0.3743% + 0.0847% = 0.459%, apparent total alkaloids.

The apparent loss upon evaporation of the chloroformic extract on a water-bath to complete dryness, leads one to suspect volatile substances, basic in character, other than alkaloids, as being present. Volatile amines have been suggested.

PROOF OF THE ABSENCE OF VOLATILE AMINES.

Method.—One hundred grams of powdered drug was treated with chloroform, followed by NH_4OH. The flask was tightly stoppered and macerated over night. Ten cubic centimeters of 28% NH_4OH was then added and the drug subjected to steam distillation. The distillate separated into chloroformic and aqueous layers. The aqueous layer was rejected; the chloroformic layer

was washed several times with water (ammonia free) and passed through absorbent cotton. It was reduced by evaporation to approximately 5 cc. and standard acid added. The residual chloroform was evaporated at water-bath temperature and the acid titrated. It showed no alkaline material whatsoever.

From this result it is concluded that volatile amines are not contributing to the variation in results.

It is not plausible to expect amines even if present in the chloroformic extract of alkaloids to nesslerize as does ammonia, but to verify this a few common amines and ammonia were nesslerized with the following results:

Methylamine HCl	(immediately)	yellow precipitate
Hexamethylenetetramine	(upon long standing)	yellow precipitate
Aniline	(upon long standing)	orange-yellow precipitate
Ammonia	(immediately)	brown precipitate
Unknown (distillate from F)	(immediately)	brown precipitate

An ammonia soap of resinous material is largely responsible for the variations noted, and is obviated only by long standing after the evaporation of the solvent or by successive additions of a solvent such as ether with spontaneous evaporation. Warming the alkaloidal residue, volatilizes the ammonia readily and does not perceptibly affect the alkaloids.

The following table is a summary of the analytical results:

U. S. P. X.

Sample.	Solvent.	Type Process.	Results.
10 Gm.	Ether-Chloroform	U. S. P. X	*a* 0.402%
			b 0.394%
			c 0.426%

MODIFIED U. S. P. X.

Sample.	Solvent.	Type Process.	Part.	Results.
				a 0.574%
		A		*b* 0.509%
				c 0.520%
10 Gm.	Ether-Chloroform			
		B		*a* 0.549%
				b 0.567%
		C		0.557%
			1	*a* 0.438%
				b 0.448%
10 Gm.	Alcohol, Ether NH_4OH (28%)	D	2	*a* 0.542%
				b 0.546%
			3	0.661%
			1	0.417%
10 Gm.	Chloroform	E	2	*a* 0.450%
				b 0.461%
			3	0.713%
10 Gm.	Ether-Chloroform	F		0.459%

ISOLATION OF ALKALOIDS.

One kilogram of drug was placed in a percolator, macerated for 18 hours with alcohol and percolated. The percolate was reduced to a viscous liquid *in vacuo*.

The semi-solid residue was extracted with water to remove the alkaloids in the form of salts as they occur in the plant. The filtered aqueous extract was reduced *in vacuo*. The residue was extracted three times with chloroform to remove any resins and chlorophyll.

After attempting crystallization of the alkaloidal extractive from ether-alcohol mixtures with negative results, the alkaloids were then removed from this solvent with diluted sulphuric acid. The alkaloids were finally recovered by shaking out with chloroform from the above solution after making alkaline with ammonia. The chloroform was evaporated spontaneously.

(*a*) To the alkaloidal residue was added 10 cc. of distilled water and gently warmed on a water-bath with continuous stirring. This aqueous extract was decanted and two other portions of water, 5-cc. and 3-cc. portions, respectively, were added to wash the residue. All three portions were combined and extracted several times with chloroform, after which the solvent was evaporated. The residue was taken up with 15 cc. of water, 2 cc. being used to rinse the container. The aqueous extract was filtered and diluted to exactly 20 cc., mixed well and polarized. A measured portion of the solution, after polarization, was evaporated and dried over calcium chloride.

$$(a)_D^{20} \quad -16.2 \text{ (water)}$$

(*b*) The portion retained by the water upon extraction with chloroform was tested qualitatively for the presence of alkaloids with positive results. It was likewise polarized as in (*a*) with the following result:

$$(a)_D^{20} \quad -16.74 \text{ (water)}$$

The specific rotations of the substance extracted by chloroform (*a*) and that remaining in the aqueous portion (*b*) indicate that they are the same, so they were combined.

A gold chloride derivative of the alkaloid was made. Large conglomerates of golden-yellow crystals formed. As far as could be detected when magnified, the crystals appeared uniform, indicating a rather pure product. Upon repeated recrystallization from hot water, long serrated crystals, together with broad yellow prisms, some having a feathery appearance under the microscope,[1] were obtained, having a melting point of 199° C. (uncor.).

There is, however, some uncertainty concerning the melting point of the aurichlorides of both the *l*- and *i*-scopolamine. Following are the results of various workers and also that recorded by two Pharmacopœias for *l*-scopolamine:[2]

E. Schmidt	212–214° C.
Kircher	208–209° C.
O. Hesse	198° C.
U. S. P. VIII	197° C.
British Pharmacopœia (1898)	198° C.

This preliminary work being done, a larger portion of drug was treated with alcohol, as in the initial extraction, using 5 Kg. of drug and the same process of purification and separation again exercised, each fraction in the process of separation being combined with the corresponding fraction of the previous lot of drug.

The portions previously polarized were below the accepted value for an aqueous solution of scopolamine, due to impurities and moisture, the latter not being com-

[1] T. A. Henry, *Plant Alkaloids*, 2nd Edition, page 88; Wilhelm Autenrieth and William H. Warren, *Laboratory Manual for the Detection of Poisons and Powerful Drugs*, 6th Edition, page 185.

[2] *American Journal of Pharmacy*, 86 (1914), 346.

pletely removed when kept in a desiccator for four days with recently fused calcium chloride. The water is probably retained by a film forming on the surface of the viscous alkaloidal residue.

To further purify the alkaloid and remove water, it was next treated with absolute ether (ether over sodium). The ethereal solution was very cloudy, indicating water, and upon the addition of anhydrous sodium sulphate the solution became clear. The ethereal solution was filtered and the ether removed by placing the solution of alkaloids in a vacuum desiccator, the vacuum being continued until the ether was removed. The fractionation with absolute ether also resulted in the separation of some resinous material which was reserved for further study.

Two separate portions were treated similarly and the optical rotation of this purified ether-soluble product resulted as follows:

1. $(a)_D^{20}$ −16.5 (alcohol) 2. $(a)_D^{20}$ −16.44 (alcohol)

The resinous substance was washed with absolute ether until the washings were negative to Mayer's Reagent and picric acid, T.S. When tested, however, with *p*-dimethylamino-benzaldehyde solution, a positive test resulted. This positive test accounts for the numerous extractions required to exhaust the drug until negative to this reagent, when the color reaction is produced not by the alkaloids, but by this resinous material, probably an alkaloidal decomposition product.

The resinous material was taken up with 0.5% H_2SO_4. The aqueous solution was rendered alkaline with NH_4OH and shaken out with $CHCl_3$ into which the brown-colored material immediately passed. Upon evaporating the chloroformic extract nearly to dryness and subsequent titration, it was found that 2.3 cc. of 0.02*N* acid was consumed. These results, then, account for the especially high results when the drug is exhausted until negative to *p*-dimethylamino-benzaldehyde and consistently higher results obtained when standard acid is added before the final chloroform is evaporated to complete dryness.

Constants obtained for this alkaloid with constants as reported by Henry, *Plant Alkaloids*, for *l*-scopolamine:

1. A thick, viscous amber-colored syrup which refused to crystallize as the base.
2. M. p. of picrate..... 188° C.
3. M. p. of aurichloride..... 199° C.
4. $(a)_D^{20}$ (*a*) −16.5 (alcohol) (*b*) −16.44 (alcohol)

Thomas A. Henry, *Plant Alkaloids*.

	Gold Chloride.	Picrate.	Specific Rotation.
Atropine	137–139	175–176	Inactive
Hyoscyamine	165	165	
Scopolamine	204–205 (uncor.)	187–188 (uncor.)	−18 in alcohol

Crystalline forms and the comparison above indicate conclusively the presence of scopolamine only in *D. innoxia*, Mill.

The usage of the term hyoscine and scopolamine has caused much confusion and controversy.[1] In Germany the names lævo- and inactive scopolamine are

[1] *American Journal of Pharmacy*, 86 (1914), 339; Allen's *Commercial Organic Analysis*, Vol. 7, 5th Edition, page 815; Merck's *Index*, 4th Edition, page 454.

employed. In England and the United States hyoscine was once used to designate the lævo- base. Preference is now given to *l*-scopolamine as the proper name.

Samples of the drug, the alkaloid, the picrate and the aurichloride have been filed for reference.

CONCLUSIONS.

1. The solvent and treatment of final chloroformic extract exert controlling influences upon the results obtained in assays.
2. The high and variable results are not attributable to volatile amines but to an ammonia soap of a resin-like material.
3. The optical rotation, crystal forms of the picrate and aurichloride and their respective melting points prove the alkaloid to be *l*-scopolamine.
4. Lævo-scopolamine was isolated, identified and was the only alkaloid found in *Datura innoxia*, Mill.

A PHYTOCHEMICAL STUDY OF GILLENIA STIPULATA.

BY L. LAVAN MANCHEY.*,[1]

Gillenia stipulata and *Gillenia trifoliata* are North American drugs indigenous to the eastern United States, known to the Indians, and used by the early colonists (1) as a substitute for Ipecac under the name American Ipecac. Of the two species the former has been generally acknowledged as the more efficacious. Although there is no botanical relation between Ipecac and American Ipecac, the roots of both plants, in being annulated, are similar; and this circumstance, no doubt, suggested to the early users of the drug a parallel in therapeutic value.

This drug received recognition in medical practice through the efforts of Barton, Schoepf and others (2, 3) and was official in the United States Pharmacopœia before the sixth revision. It was reputed to be emetic, cathartic, sudorific, expectorant and tonic (4). Ebert (5), however, states that doses of from one to twelve grains of extract prepared from drug obtained through commercial channels were entirely without effect upon himself and upon several young men. Shreeve (6), in 1835, and students (7) of the Philadelphia College of Pharmacy, in 1854, found in the root starch, gum, albumin, volatile oil, wax, fatty resin, lignin, coloring matter, gallotannic acid, lime potash and iron. Stanhope (8), in 1856, isolated a substance from the root cortex which he named "Gillenin," corroborated in 1877 by Wetherill (9). Curry (10), in 1892, reported two glucosides "Gillenin" and "Gillein," neither of which appears to be identical with "Gillenin."

EXPERIMENTAL.

For the present investigation 50-pounds of *G. stipulata*, in the form of a number twenty powder, were procured from commercial sources, and after confirming the

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* From the laboratory of Glenn L. Jenkins, Professor of Pharmaceutical Chemistry, School of Pharmacy, University of Maryland. Abstracted from a thesis submitted to the Faculty of the Graduate School of the University of Maryland in partial fulfilment of the requirements for the degree of Master of Science.

[1] Alumni Research Scholar.

identity of species a representative sample was analyzed for ash, soluble extractive, etc.

	Per Cent.		
Sample	A.	B.	Average.
Total Ash	22.03	21.95	21.99
Acid-Insoluble Ash	14.99	15.29	15.14
Moisture (corrected for volatile constituents)	7.04	7.04	7.04
Moisture by Xylene Method	6.10		
Volatile Ether-Soluble Extractive	0.54	0.43	0.48
Non-volatile Ether-Soluble Extractive	2.94	2.40	2.67
Alcohol-Soluble Extractive	6.72	6.72	6.72
Diluted Alcohol-Soluble Extractive	13.49	13.81	13.65
Water-Soluble Extractive	5.72	5.70	5.71
Petroleum Benzin Extractive	0.11	0.13	0.12

By way of preliminary examination several tests were undertaken to determine the general character of the constituents:

1. One hundred Gm. of drug, examined by the "Stas-Otto Method," gave negative tests for alkaloid and glucoside.

2. Test for alkaloid by maceration with Prollius' fluid, negative.

3. Since glucoside had been previously reported, a special search for the principle was made by treating an infusion made from 200 Gm. of the drug successively with lead acetate and lead subacetate. The filtrate from the lead precipitates together with the lead precipitates after decomposition with hydrogen sulfide were separately and carefully examined, but all tests for glucoside and saponin were negative.

4. Twenty gr. of the powdered drug when given in capsules to a small dog weighing about 3 Kg. did not produce emesis, nor did the animal evince any unnatural behaviour attributable to drug action. (Subsequently during the examination of the drug, various extractives were administered to dogs in relatively large doses, but in no case was there an apparent response to the drug.)

5. Two hundred and fifty grams of the air-dried drug in the form of a number twenty powder were extracted successively in a Soxhlet apparatus with the following liquids. After removal of the solvent the residual extracts were kept over sulphuric acid until of constant weight.

			Per Cent.
Petroleum (b. p. 35–40°)	extracted	1.30 Gm.	0.52
Ether	extracted	3.78 Gm.	1.51
Chloroform	extracted	1.43 Gm.	0.57
Alcohol	extracted	17.17 Gm.	6.87
Water	extracted	7.93 Gm.	3.13
	Total	31.61 Gm.	12.60

The petroleum extract was a yellow, fat-like semi-solid having a pleasant odor, and contained much volatile matter which was readily volatilized from paper by gentle heating. A portion of the extract was dissolved in ether and shaken first with water and then with water acidulated with hydrochloric acid. The first shakings were tested for glucoside and the second for alkaloid, but the results in both cases were negative. The ether extract was odoriferous, and both the ether and chloroform extracts were of a resinous nature.

LARGE SCALE EXTRACTION.

For the purpose of complete examination a quantity (14 Kg.) of the ground drug was extracted by continuous percolation with hot alcohol. The quantity of extract thus obtained after drying *in vacuo* amounted to 1745 Gm. Approximately

one-half (830 Gm.) of this viscid extract was set aside and reserved for future work. The remainder was mixed with water and steam was passed into the mixture until the volatile products were removed. There then remained in the distillation flask a dark colored aqueous liquid (A) and a quantity of soft, dark, resinous mass (B). The latter was collected, then washed and the washings added to the aqueous liquid.

Examination of Steam Distillate.—The first distillate was slightly opalescent and contained on the surface a small amount of oil which as distillation progressed became partly solid. It was removed with ether and the ethereal liquid dried with anhydrous sodium sulphate. Upon allowing the solvent to evaporate in a desiccator over calcium chloride under slightly reduced pressure, a small quantity of volatile oil was obtained which was insufficient for the determination of its physical constants. The reserve portion of the alcoholic extract was therefore likewise steam-distilled, and the oil thus obtained from the two portions when combined amounted to 3.6 Gm. It was of a light amber color with a slight green fluorescence; possessed an agreeable odor similar to that of the crude drug; and in alcoholic solution was neutral to litmus. Sp. gr. 25°/25°, 0.86. This relatively low value, below 0.9 (11), indicates the presence of terpenes in marked quantity. Refractive index, 1.4804. Specific rotation at 25° C., −6.39. It was soluble in 27 volumes of 75% alcohol, and upon distillation was obtained principally in two fractions, *viz.*, 85–120° and 200–240° C. The higher boiling fractions could not be distilled at ordinary pressures without decomposition.

The aqueous portion of the distillate from which the oil had been removed was faintly acid to litmus, but contained neither formic nor acetic acids.

Examination of the Aqueous Liquid (A).—The aqueous liquid, which as previously mentioned, had been separated from the soft, dark resin amounted to about four liters, and was acid to litmus. It was concentrated at a low temperature to about one-fourth this volume and then shaken many times with ether. The combined ethereal shakings were concentrated to a suitable volume and successively shaken with 3 per cent sodium carbonate and 3 per cent potassium hydroxide solutions. Both alkaline extracts were decomposed with diluted sulphuric acid and the liberated substances removed with ether. Attempts to obtain a crystalline product from the decomposed sodium carbonate and potassium hydroxide extractives by crystallization from various solvents were without success because of the high solubility of the substances. The sodium carbonate extractive, however, when sublimed at 150° C., 20 mm. pressure gave a small quantity of sublimate in the form of white needles which melted at 108–110° C. The product thus obtained was contaminated with a volatile odorous substance, since upon crystallization from petroleum benzin containing a little ether the melting point was raised to 120.5–121°. When esterified with ethyl alcohol and sulphuric acid, it formed ethyl benzoate and was thus identified as benzoic acid.

The residue from the potassium hydroxide was a brown semi-solid possessing a marked pleasant odor, and evidently consisted of a complex mixture.

The aqueous liquid (A) after the removal of the ether-soluble constituents had a reddish brown color and a sweet astringent taste becoming bitter when retained in the mouth. It gave a green color with ferric chloride and reduced Fehling's solution readily.

Test for Simple Sugar.—Detection of *d*-glucose: 5 cc. of the aqueous solution was treated with basic lead acetate solution and from the filtrate an osazone was obtained which separated from solution in five minutes, and when crystallized from alcohol melted at 204° C. It was therefore *d*-glucosazone. The remainder of the aqueous liquid was then treated with an excess of lead acetate, and to the filtrate from the lead precipitate a slight excess of basic lead acetate was added. Both lead precipitates were collected on a filter, and washed by the aid of a filter pump with a little water. The filtrate resulting from the lead precipitates, and also the lead acetate and basic lead acetate precipitates after being suspended in water were decomposed by hydrogen sulphide. To exclude the possibility of an active principle having been absorbed by the lead sulphide precipitates they were exhausted by continuous extraction with various solvents, but this treatment afforded only small quantities of inert residues. The final filtrate remaining after treatment with basic lead acetate and also the solutions resulting from the decomposition of the lead precipitates were likewise examined for an active principle by shaking them separately with chloroform. As the result of this treatment, only intractable bitter residues were obtained which were neither glucosidal nor alkaloidal in character.

The three aqueous solutions remaining from the chloroform shakings were allowed to evaporate spontaneously at room temperature until quite concentrated, and the resulting syrupy liquids separately treated with absolute alcohol. The hydroalcoholic solutions thus obtained were decanted from the precipitated matter, and subjected to fractional precipitation with ether. The final ethereal-alcoholic solutions contained practically no material in solution, and the various precipitates obtained by the foregoing procedure consisted only of sugar, tannin, pigments and some amorphous matter.

Examination of the Insoluble Resin (*B*).—This resin, which was in the form of a nearly black viscous semi-solid, was mixed with a small quantity of alcohol, distributed through Ottawa sand, and when completely dried was subjected to prolonged successive extraction in a large modified Soxhlet apparatus with the following solvents: petroleum bezin (b. p. 35–50°), ether, chloroform, ethyl acetate and alcohol.

Petroleum Benzin Extract of the Resin.—This extract was a viscous green liquid obtained after thirty-five hours of continuous percolation, and amounted to 28 Gm. The entire benzin extract was dissolved in a large volume of ether and shaken successively with ammonium carbonate, sodium carbonate and potassium hydroxide solutions. Each of the alkaline extracts was decomposed with diluted sulphuric acid, and the liberated substances removed with ether.

The decomposed ammonium carbonate extract, from which the ether had been removed upon standing over night, exhibited a readiness to sublime. The method adopted, therefore, in an attempt to isolate this volatile constituent was that of sublimation, the process being conducted at a temperature of 100° C. under 30 mm. pressure. A small quantity of sublimate, melting indefinitely between 50° and 104°, was thus collected. By repeating the process twice more and collecting the sublimate in small fractions the last fraction obtained amounted to about 50 mg. and melted sharply at 121° C. When heated with sulphuric acid and ethyl alcohol

it gave the odor of ethyl benzoate, and was therefore benzoic acid which had not been separated during steam distillation.

The quantity of sodium carbonate extractive was negligible and therefore discarded.

The decomposed potassium hydroxide extractive on the other hand amounted to several grams. No crystalline substance could be separated from it by treatment with various solvents. Consequently it was distilled at 20 mm. pressure, redistilled at 25 mm. and the fraction distilling between 100° and 250° C. collected. The presence of small quantities of a phenol were indicated by the formation of an insoluble bromine derivative and by the odor. The principal component of the mixture was a solid at room temperature, and when dissolved in a mixture of methyl alcohol and acetone and allowed to stand it separated in microscopic acicular crystals, melting at 48–49° C. In this crystalline form the compound formed a soap, and no longer possessed phenolic properties. It was precipitated in two fractions from alcoholic solution as silver salt, and analyzed.

Fraction 1:

0.0378 gave 0.0105 Ag = 27.7 per cent Ag
$C_{15}H_{35}O_2Ag$ requires 27.6 per cent Ag

Fraction 2:

0.0554 gave 0.0155 Ag = 27.9 per cent Ag
$C_{18}H_{35}O_2Ag$ requires 27.6 per cent Ag

The agreement in the analysis of the two fractions, in spite of the low melting point of the free acid, compels the decision that the compound was stearic acid in a slightly impure state.

The filtrate from the stearic acid was allowed to concentrate further until a sufficient amount of crystals separated for analysis.

Silver salt.

0.0400 gave 0.0120 Ag = 30.0 per cent Ag
$C_{16}H_{31}O_2Ag$ requires 29.7 per cent Ag

The per cent of silver found corresponds to the theoretical requirements of palmitic acid.

The mother liquor, containing the more soluble acids, afforded 0.4955 Gm. of silver salt, which upon decomposition yielded 0.0212 Gm. Ag, equivalent to 42.7 per cent Ag. $C_8H_{15}O_2Ag$ requires 42.9 per cent Ag. The more soluble portion, hence, consisted of caprylic acid or a mixture of higher and lower acids the analysis of which subscribes to these requirements.

Saponifiable and Unsaponifiable Constituents of the Petroleum Benzin Extract.—That portion of the petroleum extract which was insoluble in the solutions of the alkalies was freed from ether, and by treatment with hot 95 per cent alcohol was resolved into three fractions, namely: (I) a substance freely soluble in cold alcohol; (II) a flocculent substance soluble in hot, but less soluble in cold alcohol; (III) an insoluble viscous substance.

Fraction (1) was saponified with alcoholic potassium hydroxide, then poured into cold water and the unsaponifiable matter removed with ether. The latter solution, upon removal of the solvent, afforded a quantity of yellow oil becoming partially solid on standing. This was crystallized from a mixture of ethyl acetate

and alcohol, from which about 0.4 Gm. separated in the form of long flat plates, melting at 135°.

Upon analysis:
0.0804 gave 0.2457 CO_2 and 0.0897 H_2O; C = 83.3; H = 12.3 per cent. $C_{26}H_{44}O$ requires C = 83.7; H = 11.9 per cent.

It gave Salkowski's reaction for phytosterols, and by the Liebermann-Buchard reaction a transient violet color changing rapidly to blue, turning less rapidly to green and finally to brown.

Its acetate crystallized from acetic anhydride in long lustrous plates which melted at 121°. The compound was thus identified as a phytosterol isomeric with several compounds of the formula $C_{26}H_{44}O$ previously described in the literature (12, 13).

The insoluble flocculent substance (II), like the soluble material, was saponified, the unsaponifiable constituents removed with ether and recrystallized from ethyl acetate. A white substance, amounting to about 0.1 Gm. separated in the form of microscopic needles, melting at 78°.

Upon analysis:
0.0574 gave 0.1715 CO_2 and 0.0766 H_2O; C = 81.4, H = 14.8 per cent. $C_{30}H_{62}O$ requires C = 82.1, H = 14.3 per cent.

The compound, with bromine water, behaved as if saturated, and formed an acetyl derivative which crystallized from acetic anhydride in minute needles melting at 63–63.5°. It was thus identified as a saturated acyclic alcohol isomeric with two similar alcohols previously reported in the literature (14).

An unsaponifiable product was obtained from fraction (III) or the insoluble viscous material, but this gave no crystalline substance upon treatment with ethyl acetate and alcohol. It was distilled under reduced pressure, and found to contain a small quantity of phytosterol.

Fatty Acids.—The alkaline aqueous liquids from which the unsaponifiable constituents had been removed were combined, acidified with diluted sulphuric acid and the liberated fatty acids removed with ether. The ether was evaporated and the residue was distilled under reduced pressure. The distillate was dissolved in glacial acetic acid, decolorized with animal charcoal, and allowed to stand until a quantity of colorless crystals separated which melted at 62.5–63°. The compound was converted into the silver salt and the silver determined with the following result.

0.0868 gave 0.0256 Ag = 29.5 per cent Ag
$C_{16}H_{31}O_2Ag$ requires Ag = 29.7 per cent Ag

This result thus indicated that the substance was palmitic acid.

Ether Extract of the Resin.—This extract, as originally obtained, was a dark green ethereal solution containing a sparingly soluble amorphous substance in suspension and a more soluble viscous substance which collected on the bottom of the extraction flask as the solution cooled. The amorphous substance and the viscous matter amounting, respectively, to 6 and 7 Gm. were separately collected, leaving the soluble material which after removal of the solvent weighed 53 Gm.

The amorphous substance was not sufficiently soluble in the common organic solvents to be purified by crystallization, but by prolonged continuous extraction with hot absolute ethyl alcohol it was obtained as a perfectly white powder. It was not decomposed by diluted acids or alkalies, even on boiling. It separated from a hot 50 per cent aqueous pyridine solution, upon cooling, in an imperfectly crystalline condition. It did not contain nitrogen, and after being dried in an oven at 110° it decomposed at approximately 265°.

Upon analysis:

0.0612 gave 0.1573 CO_2 and 0.0588 H_2O. C = 70.1; H = 10.6 per cent.
0.0395 gave 0.1018 CO_2 and 0.0378 H_2O. C = 70.3; H = 10.6 per cent.

A small amount of the substance was converted into an acetyl derivative by boiling, for one hour, with acetic anhydride. The ester separated as the solution cooled, and when removed and dried, melted at 154–159°. It crystallized from ethyl alcohol in small rectangular plates, and the melting point was raised to 162°. By the Liebermann-Buchard reaction, it gave a transient pink color changing rapidly to blue and then to green.

Upon analysis.

0.0818 gave 0.2056 CO_2 and 0.0713 H_2O. C = 68.4; H = 9.7 per cent. $C_{34}H_{56}O_5$ requires C = 68.8; H = 9.5 per cent.

A portion of the acetyl derivative was hydrolyzed with alcoholic potassium hydroxide, and the liberated compound collected and analyzed. It decomposed at about 265°.

0.1123 gave 0.2957 CO_2 and 0.1087 H_2O. C = 71.8; H = 10.8 per cent. $C_{28}H_{50}O_5$ requires C = 72.0; H = 10.8 per cent.

These results were interpreted as indicating that the compound was a trihydric alcohol, $C_{28}H_{47}O_2(OH)_3$, and that the variation in percentage composition before and after acetylization might be attributable to more complete purification through hydrolysis of the acetic acid ester.

The acid constituents of the material readily soluble in ether were removed from an ether solution with diluted alkalies. Ammonium carbonate extracted small quantities of unsaturated fatty acids; sodium carbonate and potassium hydroxide only intractable resinous matter. By saponification of the residual acid-free extract an additional quantity of the phytosterol previously described was isolated, and also an acid which when crystallized from glacial acetic acid melted at 53.5°. Its silver salt was prepared and analyzed.

0.1124 gave 0.0363 Ag = 32.3 per cent Ag
$C_{14}H_{27}O_2Ag$ requires 32.2 per cent Ag

It was therefore myristic acid.

The sparingly soluble viscous substance was subjected to the same treatment as described in connection with the petroleum extract, but without success in removing any compound other than those already isolated.

Chloroform and Ethyl Acetate Extracts of the Resin.—These extracts amounted to 7 and 68 Gm., respectively. Both were brown resinous products from which no pure substance could be obtained.

Alcohol Extract of the Resin.—The alcoholic solution of this extract was poured into a large volume of water, the precipitated matter collected, dried and extracted with benzene. The benzene was allowed to evaporate spontaneously, leaving a small amount of a crystalline compound lodged in a soft resinous mass. Upon treatment with warm alcohol it remained undissolved in the form of white needles which melted with decomposition between 237° and 241°. The quantity of this substance was too small to permit further investigation.

Fusion with Potassium Hydroxide.—Fifty grams of potassium hydroxide were dissolved in 50 cc. of water in a porcelain dish, 10 Gm. of resin were added and the mixture heated until the temperature of the fused mass was 230°. It was dissolved in about 250 cc. of water, acidified with sulphuric acid and steam passed into the mixture to remove the volatile products of decomposition. Formic acid was identified in the first distillate. The liquid remaining after steam-distillation was filtered, decolorized with animal charcoal and allowed to evaporate spontaneously until a white crystalline substance separated. This compound decomposed at 197°, formed an insoluble lead salt and with ferric chloride gave a green color which turned red upon the addition of sodium carbonate, thus indicating its identity as protocatechuic acid.

Treatment with Dilute Alcoholic Sulphuric Acid.—As a final test for glucoside, a portion of the resin was hydrolyzed by boiling it for eight hours with a 5 per cent solution of sulphuric acid in alcohol. Hydrolysis did not liberate a reducing sugar and there is, therefore, no evidence of the presence of such a constituent in the drug.

SUMMARY AND CONCLUSIONS.

1. The most important constituents of the root of American Ipecac (*Gillenia stipulata*), as obtained in commerce include:

a. A volatile oil consisting largely of terpenes.

b. Water-soluble constituents.—*d*-Glucose, tannin, protocatechuic acid, benzoic acid and red coloring matter.

c. Benzin-soluble constituents.—Wax, associated with a phytosterol, $C_{26}H_{44}O$, a saturated monohydric alcohol, $C_{30}H_{62}O$, stearic and palmitic acids, small quantities of saturated fatty acids of low molecular weight and some unidentified unsaturated fatty acids.

d. Constituents removed by ether.—A trihydric alcohol, $C_{28}H_{47}O_2(OH)_3$ and myristic acid.

e. An unidentified white, crystalline compound present in the resin removed by ethyl alcohol.

2. The commercial drug contains neither alkaloid nor glucoside.

3. Although three glucosides have been reported previously by Stanhope and Curry such constituents cannot, in view of the evidence gathered from the present investigation, be regarded as components of the drug of commerce.

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DIFFERENCES IN SPECIES OF TAXUS.*

BY IVOR JONES AND E. V. LYNN.

During the course of an extended investigation into the conifers of Washington, attention was ultimately called to the western yew, *Taxus brevifolia*. This tree is little known except to the woodsmen who call it simply "yew." It inhabits the forests on the coast from central British Columbia to central California, being usually found on the shaded banks of mountain streams, deep gorges or damp ravines. Most of the thriving and finest trees occur directly under larger conifers. Whenever they are accidentally exposed to direct sunlight, the leaves acquire a yellowish brown, apparently unhealthy color. The largest specimens are encountered in Oregon and Washington, particularly on the Olympic Peninsula.

The tree attains a height of 20 to 75 feet and a diameter of 6 to 30 inches, but the growth is very slow. One specimen cut down in Washington was found to be over 100 years old, although only 4.4 inches in diameter. The trunk is straight and conical with long, slightly dropping branches which give the tree a weeping appearance. The bark is conspicuously thin, rarely over one-fourth inch thick, and covered with a layer of thin, papery, purple, easily detached scales, beneath which the newer bark is a clear rose color. There are no pitchy pockets as is characteristic of most western conifers.

The leaves, which usually remain on the branches for three or four years, are dark yellowish green on top and much paler on the under surface and are very soft to the touch. They are usually about one-half inch long and one-sixteenth inch wide. The midribs are proportionately large and prominent and the petioles are slender and yellow.

The fruit is a bright red berry which differs from that of other conifers in consisting of red pulp enclosing a single seed which is almost as large, about the size of a small pea. It becomes ripe in September and begins to fall in October.

The wood, like that of other yews, is heavy, hard, strong, brittle, closely grained and slightly resinous. It is of a light red color with a thin white sap-wood and obscure medullary rays. By the natives and pioneers it was very highly prized for bows, paddles, spears, fence posts and many other articles.

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* Scientific Section, A. Ph. A., Toronto meeting, 1932.

Of the several known species of *Taxus*, only three have been examined chemically. The bark of *Taxus canadensis* has been analyzed for moisture, ash and tannin (1). The only one which has been investigated extensively, however, is the European species, *Taxus, baccata*, together with the Asiatic variety, *Taxus cuspidata*. For centuries these have had a reputation as being toxic, although it is certain that the poisonous character is not always existent (2). At various times the seeds, fruit, leaves and young shoots have been reported as causing harmful effects in animals and man. On the other hand, the seeds are used to fatten poultry, the fruit has frequently been eaten with impunity, and cattle are known to have browsed on the shoots many times without being poisoned. The explanation of these contradictory facts is not yet certain.

A specific alkaloid was isolated by Lucas (3) in 1856 and twenty years later by Marme (4), who named it taxine. This was confirmed by Amato and Capparelli (5) in 1881, and the alkaloid was studied later by several others (6). A similar or identical base was extracted from the Asiatic yew by Ueda and Haseda (7) in 1914 and later by Kondo (8).

A glucoside, taxicatin, was extracted by Bourquelot (9) and later by Lefebre (10). The amount seemed to vary according to time of the year. A small amount of volatile oil was obtained from the needles by Amato and Capparelli (5).

The material used in the investigation of *Taxus brevifolia* was obtained from trees near the shore of Paradise Lake, twenty miles northeast of Seattle. Some of the leaves were dried in the air and some of them were used immediately. Collections were made at varying times from October 1930, to the spring of 1932.

Histological examination of the leaves and of the bark brought to light nothing unusual in cell structure. There was a complete absence of resin cells in the wood and in the tangential section was observed a spiral thickening of the vertical tracheids, far more pronounced than in other conifers with the possible exception of *Torreya*.

Volatile Oil.—Approximately 1000 Gm. of washed leaves were placed in a large flask and steam was passed through until three liters of distillate had been collected. No oil could be detected even after cohobation or after collection by means of ether, and repetitions with larger quantities of leaves were likewise fruitless. Samples of the wood and of the bark were distilled in the same way, with equally negative results. In each case the residual liquid was made acid and again distilled, but no oil could be detected at any time.

Alkaloid.—In a preliminary examination some of the leaves were extracted with ether and the ethereal solution was then exhausted with acidified water. The aqueous solution so obtained gave some precipitate with Wagner's and Mayer's reagents and with phosphomolybdic or tannic acid, but none with phosphotungstic or picric acid.

Since this left doubt as to presence of alkaloids, extracts were made from larger quantities, using four different methods. In the first the samples were macerated with ether and ammonia water (2:1). In the second the solvent consisted of very dilute sulphuric acid, while the third was similar except that fresh leaves were used in place of the dried. In each of these the extracted material was purified largely by repeated transference from aqueous to ethereal solution

in the usual way. In the fourth method the solvent consisted of boiling alcohol acidified with tartaric acid. The alcohol was ultimately evaporated under reduced pressure, the resins were removed by pouring into very dilute acid and the resulting liquid was submitted to a regular Dragendorff extraction, using petroleum ether, benzene and chloroform. After evaporating the final solvents in each method, the residues were submitted to a sodium-fusion test for nitrogen. In no instance was a positive result obtained.

In order to test efficiency of the processes, controls were made using samples of the leaves from *Taxus baccata*. All of the extracts made from ammoniacal-aqueous solutions gave decidedly positive reactions. It is safe to conclude that the leaves of *Taxus brevifolia* contain no alkaloid, or at least not more than a trace.

The experiments were repeated with other parts of the tree, especially the bark, the wood and the roots, but as before the tests were entirely negative.

Glucoside.—Approximately 500 Gm. of the leaves were digested on the steam-bath with an excess of water containing 50 Gm. of finely powdered calcium carbonate. After straining through muslin, the volume was reduced by evaporation under reduced pressure and the syrupy mass was then extracted several times with ethyl acetate, as was done by Bourquelot (9) to isolate taxicatin from *Taxus baccata*. The grayish powder so obtained amounted to 0.2 Gm. It gave none of the reactions of taxicatin and, from reduction tests before and after hydrolysis, apparently contained no glucoside.

Other extractions were made with alcohol and with water in the usual manner for isolating glucosides, but none of them gave any indications of such a substance. One cannot say positively that the leaves do not contain a glucoside, but the evidence certainly indicates that they do not.

Anthocyanins.—About 200 Gm. of the dried bark were completely extracted with hot water to give a deep red solution. Upon acidifying with hydrochloric acid, the color brightened considerably, while sodium hydroxide gave an intense greenish blue. Amyl alcohol did not extract any of the red color from an acidified solution. Nascent hydrogen from zinc dust removed the color rapidly and, as soon as the excess of zinc was filtered off, the color reappeared. All of these reactions are typical of conjugated anthocyanins.

Pectins.—Solutions of the root-bark often became very viscous and tended to gelatinize. A determination of pectic acid by the A. O. A. C. method showed 0.26 per cent in the bark.

The reasons for the striking differences in composition in the species of *Taxus* constitute a very interesting problem in plant physiology. Practically every other conifer contains a leaf oil and exudes an oleoresin, but not *Taxus brevifolia*. More peculiar yet is the absence of alkaloid and probably glucoside, both of which are characteristic of other species of *Taxus*. Significant are the facts that the western yew grows very slowly and best in the absence of direct sunlight.

SUMMARY.

Taxus brevifolia differs from other species of the genus in containing no oil, no alkaloid and probably no glucoside. The bark yields anthocyanin pigments and that of the root gives a small amount of pectic acid.

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SEATTLE, WASH.,
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STUDIES ON THE PREPARATION, TOXICITY AND ABSORPTION OF BISMUTH COMPOUNDS. V. BISMUTH COMPOUNDS OF CATECHOL, PYROGALLOL AND GALLIC ACID.*

BY W. M. LAUTER, A. E. JURIST AND W. G. CHRISTIANSEN.

The bismuth compounds of catechol, pyrogallol and gallic acid have received only a limited amount of study as anti-syphilitics. Substantially no information is available comparing them to other bismuth compounds to determine their relative toxicity and absorption. The preparation of bismuth subgallate was discussed by Schamelhout (1) and others, and other bismuth gallates by Bianquis (2) and by Sazerac and Levaditi (3), and the biological characteristics of these substances has been described by Didry (4) and by Sazerac and Levaditi (5). The preparation of bismuth compounds of catechol has been described by Weinland and Sperl (6) and by Rosenheim and Baruttschisky (7). The use of bismuth compounds of pyrogallol has been discussed by Sazerac and Levaditi (5) who studied their action as anti-syphilitics.

In this paper the preparation of several bismuth compounds of gallic acid is described and they are compared as regards their toxicity and absorption. Also the preparation of bismuth derivatives of catechol and pyrogallol is described. The latter, owing to their insolubility, were not studied to determine their toxicity and absorption because it was most unlikely that they would be readily absorbed.

TABLE I.

Compound Injected.	Medium for Injection.	Concentration Mg. Bi/Cc.	Approximate Maximum Tolerated Dose—Mg./ Bi Kg. Body Weight.	Per cent Absorption.
Sodium bismuth digallate	Water	50	Less than 400	60
Sodium bismuth digallate	Olive oil	40	Less than 400	60
Sodium bismuth methyl gallate	Olive oil	50	Less than 400	60
Sodium bismuth gallate	Water	40	Less than 40	68*

* The rats injected died in less than 72 hours.

* Scientific Section, A. PH. A., Toronto meeting, 1932.

The compounds tested were studied to determine their toxicity and absorption in the same manner as was previously employed in studying the other bismuth compounds discussed in previous publications. The compounds were injected intramuscularly into albino rats in aqueous solution or oil suspension. The absorption was determined by quantitative estimation of the unabsorbed bismuth remaining at the site of injection. The toxicity was estimated from the growth curves of the injected animals. The results obtained are given in the foregoing table.

The results show that sodium bismuth digallate is much less toxic than sodium bismuth gallate but that the absorption is not entirely satisfactory compared to the tartrates and mucates which are much more readily and completely absorbed (cf. paper II of this series). There is apparently little difference in the absorption and toxicity of sodium bismuth digallate and sodium bismuth methyl gallate whether in aqueous solution or olive oil suspension. However, these compounds are not very stable in aqueous solution since these solutions darken quite rapidly on standing. From the clinical standpoint, while sodium bismuth digallate and sodium bismuth methyl gallate are relatively low in toxicity, their slow and incomplete absorption renders them of doubtful value. Sodium bismuth gallate is not very much better absorbed but is far more toxic.

If the results described in this and previous publications are reviewed, it becomes apparent that the bismuth salts of fatty acids are relatively of the same order of toxicity as the tartrates and mucates, excepting sodium potassium bismuth tartrate which is much more toxic than the others. However, they are not nearly as completely absorbed. The iodobismuthates of the alkaloids are more toxic that the fatty acid salts, tartrates and mucates, with the sole exception of the iodobismuthate of procaine which is of the same order of toxicity as the bismuth tartrates. They are also incompletely absorbed. The bismuth compounds of thioglycollic acid are not completely absorbed, and are much more toxic than the bismuth mucates, the bismuth tartrates, the bismuth salts of the fatty acids and the bismuth compounds of gallic acid, excepting sodium bismuth gallate which is of the same order of toxicity as the thioglycollates. Sodium bismuth digallate and sodium bismuth methyl gallate are of the same order of toxicity as the tartrates but are not nearly as well absorbed. Consequently it appears that from the standpoint of toxicity and absorption, sodium or potassium tribismuth tartrate is the most satisfactory therapeutic agent of this series of compounds. However, it has been pointed out elsewhere (8) that these latter compounds are very irritating on intramuscular injection, causing severe local reactions. Therefore, it must be concluded that none of the compounds so far described in this series of studies are entirely satisfactory bismuth anti-syphilitic agents although many of them have already been used extensively in the treatment of syphilis.

EXPERIMENTAL PART.

Preparation of Sodium Bismuth Gallate.—Eleven Gm. of gallic acid were dissolved in 300 cc. of hot water and a solution of 17.6 Gm. of sodium bismuth tartrate in 300 cc. of water were added. A fine yellow precipitate was obtained which was collected on a Buchner funnel and washed with water, alcohol and

ether. When dry, the salt contained 51.52% of bismuth. Ten Gm. of this solid were then dissolved in dilute sodium carbonate solution and an equal volume of alcohol was added. A brown oil formed which became solid when treated several times with absolute alcohol. Finally, it was washed with ether. The solid contained 42.66% of bismuth and was readily water soluble, giving a dark brown solution.

The formula of this compound is $C_7H_4O_6BiNa_3$, having a theoretical bismuth content of 50.24%, showing that there was in it some bismuth digallate.

Preparation of Sodium Bismuth Digallate.—Ten Gm. of the above preparation were dissolved in 100 cc. of water and 50 cc. of bismuth subnitrate solution, prepared by diluting a solution of 150 Gm. of bismuth subnitrate in 150 cc. of concentrated nitric acid (sp. gr. 1.41) to one liter, were added. A yellow precipitate formed which was collected on a Buchner funnel, washed with water, alcohol and ether. The dry solid contained 59.7% bismuth. Ten Gm. of this were then dissolved in a dilute aqueous solution of sodium gallate. A dark oil was precipitated by the addition of acetone. The supernatant liquid was decanted and the oil was washed twice with acetone, three times with absolute alcohol which converted it into a solid, and then twice with water. The dry solid contained 32.6% of bismuth and was readily water soluble.

The formula of sodium bismuth digallate is $C_{14}H_9O_{11}BiNa_2$, having a calculated bismuth content of 28.13%. This compound was apparently a mixture containing some sodium bismuth gallate.

Preparation of Sodium Bismuth Methyl Gallate.—Ten Gm. of methyl gallate were dissolved in 150 cc. of warm water. 104 cc. of the same bismuth nitrate solution as was used above were added, and a yellow precipitate formed. This was collected on a Buchner funnel and washed with water, alcohol and ether. The water-insoluble substance contained 49.56% of bismuth. Ten Gm. of this solid were then suspended in water and a slight excess of dilute aqueous sodium hydroxide was added forming a dark red solution. Then 250 cc. of 95% alcohol were added, throwing down a fine yellow precipitate. This was collected on a Buchner funnel and washed with alcohol and ether. The readily water-soluble solid contained 49.03% of bismuth.

This substance has the formula $C_8H_9O_6BiNa_3$, containing 48.27% of bismuth.

Preparation of Bismuth Pyrogallate.—Twelve and six-tenths Gm. of pyrogallol were dissolved in 100 cc. of water and 346 cc. of a bismuth nitrate-mannite solution were added. The bismuth nitrate solution contained 48.5 Gm. of bismuth nitrate pentahydrate and an equal amount of mannite. The entire operation was carried out in an atmosphere of carbon dioxide to prevent oxidation. The yellow precipitate obtained was collected on a Buchner funnel and washed with water, alcohol and ether. The yellow solid was soluble in aqueous sodium hydroxide but was insoluble in water or sodium carbonate solution.

Calculated for $C_6H_3(OH)O_2BiOH$: Bi—59.7%; Found: Bi—59.24%.

Preparation of Bismuth Catecholate.—Thirteen Gm. of bismuth oxychloride were dissolved in 9 cc. of concentrated hydrochloric acid, and 30 cc. of saturated sodium chloride solution were added. Then saturated sodium carbonate solution

was added until a faint white precipitate was formed. The solution was then clarified and warmed, and mixed with a warm solution of 5.5 Gm. of catechol in 28 cc. of saturated sodium chloride solution. Then saturated sodium carbonate was added to the yellow solution until no further precipitate was obtained. The yellow precipitate was collected on a Buchner funnel, washed with water, alcohol and ether. The yellow solid was insoluble in aqueous sodium hydroxide but was soluble in hydrochloric acid.

The biological tests on these compounds were carried out in the Biological Laboratories of E. R. Squibb and Sons, New Brunswick, N. J.

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A STUDY OF SOME INCOMPATIBILITIES OF QUININE SULPHATE.

BY ALFRED BARTHEN, HERMAN EISENBERG AND FRANK A. LEE.

This paper is the result of a study of the incompatibilities that take place when quinine sulphate in aqueous solution is treated with any one of the following substances: Hypophosphorous acid, citric acid, acetic acid and an excess of the corresponding potassium salt is added to the mixture; also the incompatibility that results when quinine sulphate solution is treated with a solution of sodium salicylate. It has been stated that the corresponding quinine salt of the acid radical used is the substance precipitated, but in view of the fact that the acid mixture itself does not precipitate, and only after the corresponding potassium salt of the acid radical in question has been added that the actual precipitation is noticed, there is the possibility of the formation of a complex compound in each case, rather than the normal quinine salt. It was to investigate this possibility that the work was started.

EXPERIMENTAL PART.

QUININE ACETATE (1, 2).

Ten grams of quinine sulphate was added to 20 cc. of distilled water and 11 cc. of glacial acetic acid, producing a clear solution. To this solution was added 15.5 cc. of a solution of potassium acetate containing 12 Gm. of the salt. A voluminous precipitate formed immediately. The mixture was allowed to stand several hours to insure complete precipitation. The resulting precipitate was placed on a filter and washed until free from sulphates. It was dried on a porous plate and kept in a desiccator over sulphuric acid.

Qualitative tests showed that the precipitate contained the quinine and acetate radicals. When the compound was ignited, it first evolved a peculiar fruity odor. It then blackened simultaneously with the liberation of a gas. On the application of continued and higher heat, it was found that no residue remained, indicating the compound to be entirely organic.

Quantitative work showed the product to contain the percentages of quinine and acetate calculated for the salt quinine acetate.

This shows that textbooks need not be hesitant about stating the composition of the precipitate as quinine acetate.

QUININE CITRATE (3, 4, 7).

Ten and one-half grams of quinine sulphate was added to 30 cc. of distilled water containing 15.75 Gm. of citric acid: this mixture resulted in a clear solution. To this solution was added 25 cc. of a solution of potassium citrate containing 16 Gm. of the salt. A voluminous, heavy precipitate formed immediately. This was allowed to set and then filtered and washed free from sulphates. It was then dried on a porous plate and preserved in a desiccator as given under quinine acetate.

Ten and one-half grams of quinine sulphate was added to 30 cc. of distilled water containing 15.75 Gm. of citric acid: this mixture resulted in a clear solution. To this solution was added 25 cc. of a solution of potassium citrate containing 16 Gm. of the salt. A voluminous, heavy precipitate formed immediately. This was allowed to set and then filtered and washed free from sulphates. It was then dried on a porous plate and preserved in a desiccator as given under quinine acetate.

The precipitate responded positively to qualitative tests for the quinine and citrate groups. Upon ignition, the compound left no residue, demonstrating its freedom from potassium additive compounds.

Quantitative analysis showed that the substance was quinine citrate.

QUININE HYPOPHOSPHITE (4).

One hundred and fifty cc. of distilled water was added to 56.5 Gm. of quinine sulphate and 20 cc. of 50 per cent hypophosphorous acid, producing a clear solution. To this solution was added 100 cc. of a concentrated solution of potassium hypophosphite, made by dissolving 120 Gm. of potassium hypophosphite in 72 cc. of distilled water. A voluminous precipitate resulted to which was added 100 cc. of distilled water. The mixture was filtered and the residue thoroughly washed with distilled water. The precipitate was dried on a porous plate and stored in a desiccator.

The resulting compound when heated evolved a peculiar odor, and upon ignition, blackened with a liberation of the obnoxious, spontaneously combustible gas, phosphine. On further heating, the compound burned entirely without leaving a residue, demonstrating that a potassium additive compound was not formed. The substance responded to qualitative tests for quinine and for hypophosphite.

Quantitative determinations for phosphorus and quinine identified the compound as quinine hypophosphite.

QUININE SALICYLATE (5, 6).

Fourteen grams of quinine sulphate was treated with 100 cc. of distilled water; the mixture was heated to boiling and precipitated with 5.45 Gm. of sodium salicylate dissolved in 42 cc. of distilled water. The resulting material was cooled, filtered and the residue was washed free of sulphates. The product was dried and put into a desiccator.

The compound left no residue on ignition, showing that an additive compound could not have been formed. It responded to qualitative tests for the quinine and the salicylate radicals.

Quantitative work showed it to be quinine salicylate.

DISCUSSION OF RESULTS.

Considering the conditions under which the precipitates described in the experimental part were formed, it might seem possible that a complex compound in each case could be produced, especially in the first three cases. The precipitate was produced in each of these after the addition of the corresponding potassium salt. It was found, however, in all of these cases that the precipitation was probably brought about by common ion effect rather than by the production of an additive or a complex compound of some sort.

It is known that under different conditions of precipitation, such as might be found in different prescriptions, the physical character of the precipitate varies. Chemically, however, it was found to remain the same in the cases and under the conditions tried.

The results show that textbooks need not hesitate to state the composition of the precipitates that are formed as given in the foregoing report.

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Professor Olsen says, in an article on how changes occur in the practice of retail pharmacy and to make it clear that over-extensions and unjustified developments inevitably correct themselves: "Good judgment and honest common sense ultimately prevail. That's the cheering thing about the future we now face."

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DETERMINATION OF CHLOROFORM.*

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INTRODUCTION.

Several methods are given in the literature for the estimation of chloroform in Chloroform Liniment and in Spirit of Chloroform. Most of these methods involve the use of strong alkali as a hydrolyzing agent and are based on the reaction $CHCl_3 + 4KOH = 3KCl + HCOOK + 2H_2O$.

Andersen (1) used a strong alcoholic alkali solution to decompose the chloroform in Chloroform Liniment, making use of a pressure flask and also refluxing under pressure. Warren (2) permitted the liniment to stand over night in contact with 30 per cent alcoholic potash and then determined the chloride formed. Murray (3) used potassium hydroxide in methyl alcohol to decompose chloroform at room temperature. The results which he obtained were not satisfactory. Morrow (4) recommended the use of alcoholic potash to decompose the chloroform, the reaction taking place in a pressure flask. Meyer (5) and Harrison (6) determined chloroform in Chloroform Liniment by direct distillation. Willzerodt (7) also used alcoholic potash to decompose chloroform in Chloroform Liniment under pressure.

Schlicht and Austen (8) determined the chloroform in admixtures with alcohol by diluting with water and extracting with ether, then determining the specific gravity of the ethereal solution.

In our investigations three methods were used to decompose and determine the chloroform.

(1) Refluxing with strong alcoholic alkali.
(2) Refluxing under pressure.
(3) Heating with strong alcoholic alkali under pressure.

Refluxing with strong alkali and boiling under pressure gave slightly lower results than those obtained by refluxing under pressure. Not one of the three methods gave a 100 per cent recovery.

According to Mossler (9) if the conditions are not regulated the reaction between alkali in alcohol and chloroform can be as follows:

$$CHCl_3 + 3KOH = 3KCl + CO + 2H_2O$$

and it is possible for ethylene to form along with the carbon monoxide. This reaction is prevented by refluxing the chloroform with the alkali or heating under pressure. This reaction, however, should not interfere with the subsequent determination of the chloride ion.

EXPERIMENTAL.

REAGENTS REQUIRED.—*Reagent A.* Alcoholic potassium hydroxide. Dissolve 30 Gm. of reagent potassium hydroxide in 100 cc. of aldehyde free alcohol.

* Section on Practical Pharmacy and Dispensing, A. PH. A., Toronto meeting, 1933.

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Reagent B. Dissolve 25 Gm. of sodium in 200 cc. of aldehyde free alcohol.

Reagent C. Dissolve 30 Gm. of reagent potassium hydroxide in 100 cc. of isopropyl alcohol.

Silver nitrate: Tenth-normal solution.

Potassium thiocyanate: Tenth-normal solution.

Nitric acid: U. S. P. Dilute.

Ferric alum indicator: A cold, saturated solution of ferric ammonium sulphate $(NH_4)_2SO_4.Fe_2(SO_4)_3.24H_2O$ to which enough nitric acid had been added to repress the yellow color.

The same pipettes, burettes and flasks were used throughout to avoid errors.

SAMPLES USED.—*Sample A.* Chloroform, U. S. P.

Sample B. Purified chloroform.

One hundred cc. of U. S. P. chloroform was thoroughly washed with three one hundred-cc. portions of 20 per cent sodium bisulphite, then with four 100-cc. portions of distilled water. The chloroform was dried with anhydrous sodium sulphate and then distilled. This procedure was repeated three times.

SPIRIT OF CHLOROFORM.—*Sample A.* 8.8500 Gm. of Chloroform U. S. P. was accurately weighed, dissolved in alcohol and made up to 100 cc. at 25° C.

Sample B. 8.9180 Gm. of purified chloroform was accurately weighed and made up to 100 cc. at 25° C. with aldehyde-free alcohol.

Samples C and D. Spirit of Chloroform U. S. P. prepared, respectively, by Joseph Rosin and John C. Krantz, Jr.

CHLOROFORM LINIMENT.—*Sample A.* 44.200 Gm. of Chloroform U. S. P. was accurately weighed and made up to 100 cc. with Soap Liniment U. S. P. at 25° C.

Sample B. 44.3075 Gm. of purified chloroform was accurately weighed and made up to 100 cc. with Soap Liniment U. S. P. at 25° C.

ASSAY OF CHLOROFORM.—*Method I.* From a weighing burette or by means of a Victor Meyer bulb, weigh out accurately 0.2–0.5 Gm. of chloroform into a 300-cc. Erlenmeyer flask containing 50 cc. of alkali. Connect the flask with a long condenser, well cooled, and reflux on a boiling water-bath for four hours. (The connecting stopper must be wrapped in tin foil.) Cool, transfer to a 500-cc. volumetric flask and make up to volume with distilled water. Place a 100-cc. aliquot in a 250-cc. beaker and evaporate on a water-bath until all the alcohol is removed, add a few drops of phenolphthalein, and acidify with dilute nitric acid. Transfer to a 250-cc. volumetric flask and add 40 cc. of 0.1 normal silver nitrate solution. Shake the stoppered flask until the precipitate coagulates enough to give a clear supernatant liquid. Make up to the mark, mix, and filter through a dry filter, discarding the first 15 cc. of filtrate. Transfer 100 cc. of the filtrate into a beaker, add 2–3 cc. of ferric alum indicator and titrate the excess silver nitrate with tenth-normal potassium thiocyanate. Carry out a blank determination using the same amounts of reagents, and apply a correction for the end-point and the chloride in the reagents. Each cc. of tenth-normal silver nitrate consumed is equivalent to 0.00398 Gm. of chloroform.

Method II. Weigh accurately 0.2–0.5 Gm. of chloroform into a 500-cc. Erlenmeyer flask containing 50 cc. of alkali. Stopper the flask with a foil-covered rubber stopper carrying a U-shaped condenser and wire the stopper securely. To guard against danger from bursting, cover the flask with a towel. Connect the condenser to a cold water supply and heat the flask on a water-bath for three hours. Complete the determination as in Method I.

The U-shaped condenser: A piece of glass tubing with an outside diameter of 7 mm. and 30 cm. long is heated and bent double, the radius of the bend being about one cm. The ends are fire polished and pushed through a two-hole rubber stopper so that the length of the condenser from the top of the rubber stopper to the end of the bend is about 12 cm. The open ends are reheated and bent away from each other.

Method III. This method was the same as Method I except that a pressure bottle of 225 cc. capacity was used in place of the Erlenmeyer flask and condenser.

The chloride formed in the above reactions was also determined gravimetrically according to the usual procedure, filtering through a Gooch crucible and drying the precipitate at 110° C., using 100-cc. aliquots in each determination. The re-

sults obtained gravimetrically and volumetrically checked quite well, but the volumetric methods are preferred, due to the shorter time required for the operation.

TABLE I.—DETERMINATION OF CHLOROFORM.

Each Value Given Is the Average of Four Determinations on Aliquot Samples.
(Volumetric Determination of Chloride.)

Sample.	Method.	Reagent.	Weight of Sample.	Gm. Recovered.	Per Cent.
A	I	A	0.5438	0.5353	98.43
A	II	A	0.4108	0.3897	97.27
A	III	B	0.4570	0.4399	96.27
A	I	C	0.3012	0.2945	97.77
A	II	B	0.4562	0.4485	98.32
B	I	A	1.0581	1.0445	98.66
B	I	A	0.3690	0.3670	99.42
B	I	B	0.8333	0.8204	98.45
B	I	B	0.2824	0.2806	99.39
B	I	C	1.8225	1.7498	96.03
B	II	A	2.1106	2.0784	98.57
B	II	A	0.4973	0.4939	99.28
B	II	B	0.3543	0.3515	99.28
B	II	C	0.2980	0.2887	96.71
B	III	A	1.1611	1.1283	97.40
B	III	A	0.3858	0.3818	98.84
B	III	B	0.2933	0.2897	98.70

TABLE II.—DETERMINATION OF CHLOROFORM.

(Gravimetric Determination of Chloride.)

Sample.	Method.	Reagent.	Sample Used.	Weight Recovered.	Per Cent.
B	I	A	1.0581	1.0401	98.39
B	I	B	0.8337	0.8072	96.82
B	I	C	1.6613	1.6107	96.95
B	II	A	1.8067	1.7679	97.28
B	II	B	0.3427	0.3353	97.84
B	II	C	0.2288	0.2211	96.63
B	III	A	1.1604	1.1372	98.00
B	III	B	1.0495	1.0235	97.61
B	III	C	1.1933	1.1648	97.61

CHLOROFORM LINIMENT.—*Method I.* Measure accurately by means of a pipette 5 cc. of chloroform liniment at 25° C. into a 100-cc. volumetric flask containing alcohol. Add enough alcohol to make up to volume at 25° C. and mix thoroughly. By means of a pipette transfer 10 cc. of the diluted sample into a 300-cc. Erlenmeyer flask containing 50 cc. of the alkali solution. Connect the flask with a well-cooled reflux condenser and heat on a water-bath for four hours. Complete the assay as in Method I under chloroform.

Method II. Measure accurately 10 cc. of chloroform liniment at 25° C. into a 100-cc. volumetric flask containing alcohol, make up to volume and mix thoroughly. By means of a pipette transfer 10 cc. of the dilute sample into a large hard glass test-tube containing 20 cc. of distilled water and 5 cc. of sulphuric acid. Connect the tube with a water-cooled condenser and heat gently until about 10 cc. are distilled over into a 300-cc. Erlenmeyer flask containing 50 cc. of alcoholic alkali. Surround the Erlenmeyer flask with an ice-bath during the distillation. All rubber stoppers must be covered with tin foil.

Connect the flask containing the distillate and the alkali with a reflux condenser and heat on a water-bath for four hours. The remainder of the procedure is the same as in Method I under chloroform.

TABLE III.—DETERMINATION OF CHLOROFORM IN CHLOROFORM LINIMENT.

(Average of Four Determinations.)

Sample.	Method.	Reagent.	Gm. Found/100 Cc.	Per Cent Recovery.
B	I	A	43.4180	98.00
B	I	B	43.4420	98.04
B	IA*	A	43.4700	98.10
B	IA	B	43.4620	98.09
B	IB[1]	A	43.4880	98.15
B	IB	B	43.3800	97.90
B	II	A	43.4040	97.96
B	II	B	43.3806	97.91
B	IIA	A	43.5966	98.39
B	IIA	B	43.5788	98.35
B	IIB	A	43.4878	98.15
B	IIB	B	43.5808	98.36
A	I	A	43.0000	97.28
A	I	B	42.4640	96.07
A	IA	A	41.5200	94.00
A	IA	B	41.5060	93.90
A	IB	A	42.8600	96.98
A	IB	B	42.8940	97.04
A	II	A	43.4400	98.28
A	II	B	43.0800	97.46
A	IIA	A	43.4800	98.37
A	IIA	B	43.3070	97.97
A	IIB	A	43.2400	97.82
A	IIB	B	43.5330	98.50

* In Methods IA and IIA a pressure bottle was substituted for the flask and reflux condenser.

[1] In Methods IB and IIB a flask containing a U-shaped condenser was used.

TABLE IV.—CHLOROFORM IN SPIRIT OF CHLOROFORM.

(Average of Five Determinations.)

Sample.	Method.	Reagent.	Cc. Sample.	Gm. $CHCl_3$.	Gm./100 Cc.	Per Cent Recovery.
D	I	A	5	0.4221	8.442	.....
C	I	A	5	0.4181	8.362	.....
A	I	A	5	0.4243	8.486	95.84
A	II	A	5	0.4249	8.498	96.02
A	III	A	5	0.4263	8.526	96.39
A	I	C	5	0.4099	8.198	92.64
A	II	C	5	0.4226	8.452	93.90
A	III	C	5	0.4104	8.208	92.77
A	I	B	5	0.4271	8.542	96.52
A	II	B	5	0.4152	8.304	93.80
A	III	B	5	0.4238	8.476	95.77
B	I	A	5	0.4383	8.766	98.32
B	II	A	5	0.4398	8.796	98.63
B	III	A	5	0.4390	8.780	98.45
B	I	C	5	0.4223	8.446	94.72
B	II	C	5	0.4251	8.502	95.35
B	III	C	5	0.4271	8.542	95.55
B	I	B	5	0.4404	8.808	98.79
B	II	B	5	0.4394	8.788	98.28
B	III	B	5	0.4397	8.794	98.73

CHLOROFORM IN SPIRIT OF CHLOROFORM.—The methods used to determine chloroform in Spirit of Chloroform were the same as those used to determine chloroform. Samples of Spirit of Chloroform were taken as follows: Five cc. were transferred accurately with a pipette into the flask containing alkali and hydrolysis effected. The samples were all withdrawn at 25° C.

From our experience, we find that one of the greatest sources of error lies in the sampling of the liniment and Spirit of Chloroform due to the loss of chloroform because of its volatility. All samples were withdrawn at a temperature of 25° C. In measuring chloroform liniment care should be taken that none of the liniment touches the sides of the flask but instead the tip of the pipette must be kept submerged in the alcohol. Also in measuring the samples a measuring pipette should be used rather than a transfer pipette. In refluxing, the condensers must be well cooled and all rubber stoppers must be wrapped in tin foil.

SUMMARY AND CONCLUSIONS.

Method I is preferred for the assay of Spirit of Chloroform. With a well-cooled condenser of proper length (the Allihn type with the condensing tube consisting of a series of bulbs is preferred) and an approximately 5 normal alcoholic solution of potassium hydroxide, there is very little danger of loss of chloroform during hydrolysis. Equally good results are obtained by performing the hydrolysis under pressure, but the special apparatus required and the attendant dangers resulting from operations under pressure make these methods of less convenience. A recovery of 98.32% is obtained by this method, which is well within the allowable limits for the chloroform content of Spirit of Chloroform.

By diluting chloroform liniment to ten times its volume with alcohol, and mixing 10 cc. of this dilution with 20 cc. of water and 5 cc. of sulphuric acid before distilling, the chloroform is completely removed in the first 10 cc. of distillate and is completely retained by 50 cc. of the alcoholic alkali. The same conditions govern completeness of hydrolysis and loss of chloroform as in the assay of the spirit. An average recovery of 98.12% is obtained, as compared with an average recovery of 97.64% by direct hydrolysis of the diluted liniment. The presence of fatty acid during direct hydrolysis causes a loss in recovery of approximately 0.6%.

It is believed that direct hydrolysis of Spirit of Chloroform with alkali under a reflux condenser, and distillation of diluted chloroform liniment followed by alkaline hydrolysis under a reflux condenser are of sufficient convenience and accuracy to warrant their adoption as Pharmacopœial methods of assay.

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PITTSBURGH, PA.
August 16, 1932.

ASSAY METHODS FOR SOME N. F. VI PREPARATIONS CONTAINING BROMIDES.*

BY DONALD C. GROVE AND EDWARD M. HOSHALL.

There are six preparations containing bromides proposed for admission to the N. F. VI, namely, Elixir of Ammonium Bromide, Elixir of Potassium Bromide, Elixir of Sodium Bromide, Elixir of Three Bromides, Elixir of Five Bromides and Syrup of Five Bromides. As these preparations are quite frequently prescribed by physicians, there is certainly no question as to the need of accurate methods of analysis.

The method of assay proposed below is the U. S. P. X method for the determination of bromides, which has been modified to apply to the N. F. preparations. All quantities given in the assay method are based on the formulas of these preparations as they will appear in the N. F. VI.

(*a*) As Elixir of Potassium Bromide, Elixir of Ammonium Bromide and Elixir of Sodium Bromide are all to contain the same quantity of the respective bromide (25 Gm. per 100 cc.) the following method may be applied to each.

Assay Method.—Dilute 10 cc. of the elixir to 200 cc. Introduce into an Erlenmeyer flask 25 cc. of the diluted elixir, 50 cc. of 0.1*N* silver nitrate, 2 cc. of nitric acid and 2 cc. of ferric ammonium sulphate T.S. in the order named and determine the excess silver nitrate by titrating with 0.1*N* ammonium thiocyanate until the supernatant liquid remains reddish brown in color after it is well shaken. The difference between the number of cc. of 0.1*N* silver nitrate and the number of cc. of 0.1*N* ammonium thiocyanate multiplied by the equivalent of the respective bromide represents the number of Gm. of bromide in 100 cc. of the elixir.

$$\text{Equivalent for Elixir of Ammonium Bromide} = \left(0.009796 \times \frac{200}{25} \times 10\right) = 0.78368.$$

$$\text{Equivalent for Elixir of Potassium Bromide} = \left(0.011902 \times \frac{200}{25} \times 10\right) = 0.95216.$$

$$\text{Equivalent for Elixir of Sodium Bromide} = \left(0.010292 \times \frac{200}{25} \times 10\right) = 0.82336.$$

EXPERIMENTAL.

Before making up any of the preparations, it was necessary to run an analysis on each salt so that from the per cent purity of the salt, the exact amount of bromide that should be recovered in the preparation could be calculated. All the salts were assayed for bromide by the U. S. P. X method with the following results:

TABLE I.

	Analyst A. Total Bromide.			Analyst B. Total Bromide.			
Salt.	1.	2.	Ave.	1.	2.	Ave.	Ave. A & B.
NH_4Br	100.38%	100.14%	100.26%	100.41%	100.36%	100.39%	100.32%
KBr	99.68%	99.64%	99.66%	99.58%	99.48%	99.53%	99.60%
NaBr	101.20%	101.32%	101.26%	101.43%	101.50%	101.47%	101.36%

The high results obtained in the case of ammonium bromide and sodium bromide were due to the presence of small amounts of chloride. Most manufacturers allow a tolerance of 0.6% chloride in C.P. and reagent bromides, some as

* From the laboratories of Glenn L. Jenkins, University of Maryland, School of Pharmacy.

high as 1.5%. Theoretically a sample of sodium bromide containing 0.6% sodium chloride assay by the U. S. P. X method should assay 100.46% sodium bromide, or if it contained 1.5% sodium chloride it should assay 101.44% sodium bromide.

Elixir of Ammonium Bromide, Elixir of Potassium Bromide and Elixir of Sodium Bromide were carefully prepared with the assayed salts and were assayed by the method given above. The results of analysis are as follows:

TABLE II.

	Analyst A.					Analyst B.				
	Total Bromide.					Total Bromide.				
Prepara-tion.	1. Gm./-100 cc.	2. Gm./-100 cc.	Ave.	Theo-retical Gm./-100 cc.	% error.	1. Gm./-100 cc.	2. Gm./-100 cc.	Ave.	Theo-retical Gm./-100 cc.	% error.
Elixir KBr	24.891	24.851	24.871	24.900	−0.1	24.802	24.742	24.772	24.900	−0.8
Elixir NaBr	25.216	25.241	25.229	25.340	−0.4	25.148	25.173	25.161	25.340	−0.7
Elixir NH_4Br	24.849	24.865	24.857	25.080	−0.9	24.963	24.898	24.931	25.080	−0.6

The average result of both analysts A & B for the salts (see Table I) was used to calculate the theoretical number of Gm. of bromide per 100 cc. In all cases the error was less than 1% for each analyst.

In the proposed formulas for the above elixirs the N. F. allows the dispenser to color the elixir if he so desires by adding 1.5 cc. of compound tincture of cudbear per 100 cc. Accordingly, samples of the three elixirs containing cudbear were assayed and results similar to those above were obtained, all within 1% of error showing that the color does not interfere with the assay method.

(*b*) Elixir of Three Bromides, Elixir of Five Bromides and Syrup of Five Bromides may all be assayed by the method given below.

Assay Method.—Dilute 10 cc. of the elixir or syrup to 300 cc. Use an aliquot of 50 cc. and continue the assay as in (*a*) beginning with the words "introduce into an Erlenmeyer flask."

$$\text{Equivalent for Elixir of Three Bromides} = 0.01059 \times \frac{300}{50} \times 10 = 0.6354.$$

$$\text{Equivalent for Elixir of Five Bromides} = 0.01037 \times \frac{300}{50} \times 10 = 0.6222.$$

$$\text{Equivalent for Syrup of Five Bromides} = 0.01058 \times \frac{300}{50} \times 10 = 0.6348.$$

EXPERIMENTAL.

In making the above preparations it was necessary to analyze two more salts. The results of analysis of calcium bromide and lithium bromide are as follows:

TABLE III.

	Analyst A. Total Bromide.			Analyst B. Total Bromide.			
Salt.	1.	2.	Ave.	1.	2.	Ave.	Ave. A & B.
$CaBr_2$	81.40%	81.34%	81.37%	81.27%	81.47%	81.37%	81.37%
LiBr	85.21%	85.27%	85.24%	85.23%	85.19%	85.21%	85.23%

Elixir of Three Bromides, Elixir of Five Bromides and Syrup of Five Bromides were carefully prepared with the assayed salts, and assayed by the method above. The results of analysis are as follows:

TABLE IV.

Preparation.	Analyst A. Total Bromide. 1. Gm./-100 cc.	2. Gm./-100 cc.	Ave.	Theoretical Gm./-100 cc.	% error.	Analyst B. Total Bromide. 1. Gm./-100 cc.	2. Gm./-100 cc.	Ave.	Theoretical Gm./-100 cc.	% error.
Elixir 3 Br	23.955	23.968	23.962	24.102	−0.6	23.968	23.949	23.959	24.102	−0.6
Elixir 5 Br	24.969	24.932	24.952	24.852	−0.4	24.950	24.925	24.938	24.852	+0.3
Syrup 5 Br	23.629	23.603	23.616	23.809	−0.8	23.603	23.654	23.629	23.809	−0.8

Both analysts obtained results under one per cent of error.

CALCULATIONS.

In calculating the amount of bromide equivalent to one cc. of 0.1*N* silver nitrate in Elixir of Three Bromides, Elixir of Five Bromides and Syrup of Five Bromides the following general formula was developed and used:

$$F = \frac{a}{\frac{b_1}{c_1} + \frac{b_2}{c_2} + \frac{b_3}{c_3} + + + + +}$$

Where F = number of Gm. of mixed bromides equivalent to 1 cc. 0.1*N* $AgNO_3$.
a = total number of Gm. of bromides (based on 100% purity) in mixture.
b_1, b_2, b_3, etc. = number of Gm. of individual bromides (100% pure) in mixture.
c_1, c_2, c_3, etc. = number of Gm. of the bromide represented by b_1, b_2, b_3, etc., equal to 1 cc. *N*/10 $AgNO_3$.

The factor for Elixir of Three Bromides, which contains 80 Gm. of sodium bromide, 80 Gm. of ammonium bromide and 80 Gm. of potassium bromide per liter of solution, is calculated thus:

$$F = \frac{240}{\frac{80}{0.010292} + \frac{80}{0.011902} + \frac{80}{0.009796}} = 0.01059$$

The factor for Syrup of Five Bromides is calculated as follows: The syrup contains 80 Gm. of potassium bromide, 80 Gm. of sodium bromide, 50 Gm. of ammonium bromide, 25 Gm. of calcium bromide and 8 Gm. of lithium bromide per liter of solution. Thus substituting in the formula:

$$F = \frac{237.8}{\frac{80}{0.011902} + \frac{80}{0.010292} + \frac{50}{0.009796} + \frac{25 \times 0.84}{0.009996} + \frac{8 \times 0.85}{0.008686}} = 0.01058$$

According to the U. S. P. X, calcium bromide should contain at least 84% of $CaBr_2$, thus we have to multiply 25 Gm. by 84% to get the amount of 100% $CaBr_2$ present. The same applies to lithium bromide, the N. F. V allows a minimum of 85% LiBr.

The calculations for Elixir of Five Bromides are carried out similar to those above, F being equal to 0.01037.

SUGGESTED STANDARDS.

Elixir of Potassium Bromide, Elixir of Sodium Bromide and Elixir of Ammonium Bromide each should contain not less than 24.5 Gm. nor more than 25.5 Gm. of the respective bromide per 100 cc. of elixir. This allows a tolerance of 2% above and 2% below the amount specified in the formula.

Elixir of Three Bromides should contain not less than 23.4 Gm. nor more than 24.6 Gm. of total bromide per 100 cc. of elixir. This allows a tolerance of 2.5% above and 2.5% below the amount specified in the formula.

Elixir of Five Bromides should contain not less than 24.52 Gm. or more than 25.78 Gm. of total bromide per 100 cc. of elixir. This allows a tolerance of 2.5% above and 2.5% below the amount of pure bromides specified in the formula.

Syrup of Five Bromides should contain not less than 23.19 Gm. nor more than 24.37 Gm. of total bromides per 100 cc. of elixir. This allows a tolerance of 2.5% above and 2.5% below the amount of pure bromides specified in the formula.

CONCLUSION.

Elixir of Potassium Bromide, Elixir of Sodium Bromide, Elixir of Ammonium Bromide, Elixir of Three Bromides, Elixir of Five Bromides and Syrup of Five Bromides can be accurately assayed by the U. S. P. X (Volhard) method for assay of bromides.

It is recommended that the assay methods as given above, with the suggested standards be adopted in the N. F. VI.

DETAILING THE DENTIST FOR HIS PRESCRIPTIONS.*

BY A. O. MICKELSEN.[1]

Dentistry has made astounding advancements. It is now a recognized branch of the medical profession, requiring at the present time five years of college training—four years of which must be devoted to the study of subjects relating directly to the profession.

Such subjects as anatomy, histology, bacteriology, pathology, bio-chemistry, surgical anatomy, anesthesia, principles of surgery, clinical medicine, materia medica, pharmacology, physiology and physical diagnosis have given the dentist a good foundation for the diagnosis and treatment of most pathological conditions of the oral cavity. The disturbances of the oral cavity that lie within the province of the clinical practitioner are primarily of an infectious nature, requiring a more or less specific treatment for each individual case. Directed care is necessary as the mouth, throat and nose are the avenues through which pathogenic bacteria gain entrance into the body, causing serious diseases.

Instead of directed medication by the dentist, the patient is instructed to purchase some drug or patent preparation and treat himself. However, the dentist is not solely to blame for this condition; there are numerous preparations on the market prepared especially for the convenience of the dentist and the patient. These are the directions accompanying such a preparation, not mentioning the trade name: Quoting—"*Directions*—to relieve distress and discomfort due to simple headache, head colds, simple neuralgia and muscular aches and pains, also after tooth extraction, and for painful menstruation. In such conditions 1 and 2 tablets should be taken with a half glass of water and repeated 1 tablet in an hour if necessary." Those are the directions accompanying this sample to aid the

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* Section on Practical Pharmacy and Dispensing, A. PH. A., Toronto meeting, 1932.

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patient in the treatment of perhaps a most serious ailment. Right here community diagnosis and treatment have started. These samples are distributed gratuitously to dentists with a cloak of aiding the busy dentist. The real purpose back of such generosity by the manufacturer is to increase self medication by selling directly to the public without the direction of professional knowledge.

The advertising quoted from this package is both deceptive and misleading to the individual not having a knowledge of medicine and human physiology. To illustrate the confidence which the laity have in such preparations distributed through the dentist—a lady announced at an afternoon party that her dentist had given her a sample of this preparation, which she was using as a general home remedy. She wanted to spread the news to her friends that they too might take advantage of this new beneficial preparation. She relied on the statement following the directions on the same package: Quoting from the same container: "Each drug has a particular action of its own, and combined, they have a synergistic action which insures maximum relief. . . . is non-narcotic and non-habit forming. . . . is a febrifuge, which means that it should reduce fever. . . . is safe, does not harm the heart and will not upset the stomach." Medication of this sort is neither sound nor professional and is intended solely for a commercial transaction, disregarding the injury to public health.

Such advertising, as brought out by the survey on the Costs of Medical Care, is costing the people of the United States $525,000,000.00 annually for self medication, in contrast to only $190,000,000.00 annually spent for directed medication—only 27% of the total expenditure is directed medication.

Unless the physicians, dentists and pharmacists coöperate in a professional way, the practice of internal medicine is going to retrograde from a profession to any man's business, resulting in a public health menace. Figures in dollars cannot be obtained with reference to the cost of self medication breaking down the health of our nation, but it is conceded by those who are in a position to know, that self medication is neither economically sound nor the logical method to restore or retain your health.

Medicine to be of value to the individual must be more or less specific in its action. The amount to be taken must be determined by the dentist directing its use. This can only be controlled by the writing of a prescription. Referring to the quoted statement, namely, that "It is safe, does not harm the heart and will not upset the stomach." This is true of no drug having a marked physiological action. A drug with a marked physiological action is not free from injury to the health if repeated often and further, in doing so, a habit is formed which may result in a loss of health beyond the power of medicine to restore. Medicine to serve its purpose must be directed by the professional man and this can be brought about only by an original prescription written by the doctor. The prescription will not take on the cloak of a trade name which can be memorized by the patient and his friends. Lay diagnosis and medication are thus discouraged, nor will such prescriptions find their way into the magazines or radio programs. The chance for self-medication is minimized, because professional knowledge is required to write, interpret and fill prescriptions.

Medication by prescriptions is an advantage to the patient, doctor, pharmacist and pharmaceutical manufacturer. To the patient it may seem more costly at

the time, but he is taking no chance of injuring the most precious thing possessed—Health. Directed medication carries with it a professional interest in behalf of the patient, from both the dentist and the pharmacist. When beneficial effects of the prescription have been exhausted, there is a professional knowledge to advise discontinuing further use. To the dentist who prescribes for his patients and safeguards their health, there is an added professional pride, professional duty and self-confidence. Directed medication requires repeated returns by the patient for treatment and direction. This enables the pharmacist to practice his profession—coöperating with the doctor and his patient. The pharmaceutical manufacturer is insured continued ethical business. Preparations intended solely for commercial transactions can only have a short duration in the treatment of human ailments.

Those who do the world's work must be able to determine the work to be done. This is perhaps more true of the professions than it is of the trades, as so much depends upon ethical practice. As professional pharmacists, it is our duty to coöperate with the dental profession. Detail the dentists in your respective location and ask them to coöperate in a professional way by treating their patients by directed medication—through prescriptions. Furnish the dentist with efficient and correct information concerning the action of drugs they wish to use. Invite the dentists into your prescription department, become better acquainted. Dental preparations are new and varied, and it may require several visits for a mutual understanding. Furnish the dentist with several prescriptions, completely written out for his guidance or better still filing cards containing prescription detail information. Teach the dentist prescription writing in a tactful manner.

A great deal of prescription writing by the dentist is imperative in the future because he is holding a higher professional position than before, and has much more advanced professional training. Do not hesitate to detail the dentists. I know them to be receptive and willing to coöperate for the advancement of the dental profession. I believe it is fundamentally sound that the dentist should treat cases by direct medication—prescriptions—which are at the present time receiving little or no professional attention.

It was my pleasure to present this subject before the Oregon State Pharmaceutical Association, with the result that the Association pledged its support in furtherance of this movement. Since the convention, I have received letters from pharmacists, stating that their results were most gratifying in detailing dentists.

North Pacific College of Oregon, School of Dentistry, is supporting this movement by requiring prescription writing by their junior and senior students.

I earnestly recommend that the colleges of pharmacy include dental prescriptions and preparations in their pharmacy laboratory courses that they may become better acquainted with the needs of the dental practitioner.

1934 MEETING OF INTERNATIONAL RED CROSS SOCIETY.

The 15th conference of the International Red Cross Society will be held in Tokyo, Japan, next year. This decision was reached by the Executive Committee of the International Red Cross Society which met in Brussels, Belgium, on March 31st. According to the decision of the committee, the proposed conference at Tokyo will meet October 20, 1934.

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

"The following list of drugs prepared by the Committee on Materia Medica of the Joint Conference of Boards and Colleges of District No. 2 is sure to be of great interest to members of state boards of pharmacy and to teachers of materia medica. Whether or not the boards of pharmacy accept this list, the Committee deserves our thanks and appreciation for the great amount of work they have done in preparing it. Your Editor, not being a teacher of materia medica, probably has no right to criticize the work of this Committee. However, it does seem to me that the rating (55%) given to vegetable and animal drugs is high. Should not students know something of the method of obtaining many of the drugs, such as oil of bitter almond, acacia, oil of turpentine, etc.? And should students not also have an understanding of the meaning of such terms as oleoresin, balsam, fixed oil, alkaloid, etc.? Perhaps the Committee intends that this should all be included under 'Official Definition of the Drug' but it is not so stated.

"Every teacher of materia medica is urged to give this list his careful consideration, and every state board of pharmacy should also study it. Perhaps out of this movement may come the selection of a list that will be satisfactory to all state boards of pharmacy."—C. B. JORDAN, *Editor*.

SCOPE OF EXAMINATION IN MATERIA MEDICA AND LIST OF DRUGS.

RECOMMENDED BY THE COMMITTEE ON MATERIA MEDICA AND APPROVED BY THE CONFERENCE OF STATE BOARDS AND COLLEGES OF N. A. B. P., DISTRICT NO. 2, AS A LIST TO WHICH STATE BOARD QUESTIONS IN MATERIA MEDICA SHOULD BE RESTRICTED.

The joint meeting of the Members of State Boards of Pharmacy and Delegates of the Faculties of Colleges of Pharmacy of District No. 2 have adopted a code delimiting the scope of the State Board examination in Materia Medica, together with a list of drugs to which the State Board exmination is to be limited. This list is not intended to restrict in any way the subjects or drugs which the teacher of Materia Medica may desire to discuss with his classes but is for the guidance of the State Boards of Licensure.

Three State Boards have already formally accepted these recommendations and have agreed to limit their examinations in Materia Medica to the drugs recommended on the list. It is obviously desirable that there be some general recognition of what the candidate for pharmaceutical licensure should be expected to know. In the hope that this list may be adopted by other states, or at least furnish a basis for a discussion looking toward the adoption of a national agreement, the Conference of District No. 2 has authorized the publication of the material herewith presented. The Committee on Materia Medica responsible for this outline consisted of the following: G. A. Bunting, William Mansfield and J. M. Woodside, representing the State Boards; C. W. Ballard, J. R. Minehart (since deceased) and H. C. Wood, Jr., representing the colleges.

1. GENERAL SCOPE OF THE EXAMINATION.

The examination in Materia Medica should cover the following topics:

1. Nomenclature (including Latin and English official titles and commonly used synonyms).
2. Official definitions (including botanic or zoölogic origin).
3. Appearance and physical properties. Under "appearance," as applied to vegetable drugs, is meant especially macroscopic appearance.

4. Dosage of drug and its important preparations.
5. Therapeutic action or uses.
6. Names of important active principles.
7. Methods of storing drugs subject to deterioration on keeping.
8. Definitions of common medical terms, such as those defining drug action, or the names of common diseases.
9. The symptoms and treatment of the more common poisonings.

It is suggested that the relative frequency of questions on these topics might be divided about as follows:

Nomenclature	15%	Miscellaneous	5%
Official definitions	15%		100%
Appearance, etc.	5%		
Dosage	25%	Organic chemicals	20%
Active principles	5%	Inorganic chemicals	15%
Therapeutic action	10%	Vegetable and animal drugs	55%
Medical terms	10%	Serums and glandulars	10%
Toxicology	10%		100%

LIST OF DRUGS.

Acacia
Acetanilidum
Acetonum
Acetphenetidinum
Acidum Aceticum
Acetylsalicylicum
Acetyltannicum
Benzoicum
Boricum
Bromauricum
Citricum
Hydriodicum
Hydrochloricum
Hydrocyanicum Dil.[1]
Hypophosphorosum
Nitricum
Oleicum
Phosphoricum
Salicylicum
Stearicum
Sulphuricum
Tannicum
Tartaricum
Aconitum
Acriflavine[1]
Adeps
Lanæ
Aether
Aether Aceticus
Aethylis Aminobenzoas
Chaulmoogras
Chloridum
Nitris
Aethylmorphinæ Hydrochloridum
Agar
Alcohol
Allium
Alœ
Althæa
Alumen
Alumini Chloridum
Alumini Sulphas
Amidopyrina
Ammonii Bromidum
Carbonas
Chloridum
Hydroxidum
Hypophosphis
Iodidum[1]
Salicylas
Valeras
Amylis Nitris
Amylum
Anethol
Anisum
Antimonii et Potassii Tartras
Antimonii Oxidum
Antipyrina
Apocynum
Apomorphinæ Hydrochloridum
Aralia
Argenti Nitras
Argento-Proteinum
Arnica
Antitoxinum Diphthericum
Antitoxinum Tetanicum
Arseni Iodidum
Arseni Trioxidum
Arsphenamina
Asafœtida
Aspidium
Balsamum Peruvianum
Barbitalum
Barbitalum Solubile
Barii Sulphas
Belladonna
Benzoinum
Betanaphthol
Bismuthi Subcarbonas
Subgallas
Subnitras
Subsalicylas
Bitumen Sulphonatum
Bryonia
Buchu
Caffeina
Caffeina Citrata
Calamina Præparata
Calcii Bromidum
Carbonas Præcipitatus
Creosotas[1] (Calcreose)
Glycerophosphas
Hypophosphis
Iodobehenas
Lactas
Lactophosphas
Phosphas Præcipitatus
Calumba
Calx
Calx Chlorinata
Camphora
Camphora Monobromata[1]

[1] Not official in either the U. S. P. or N. F.

Cannabis
Cantharis
Capsicum
Carbo Animalis Purificatus
Carbo Ligni
Carbonei Tetrachloridum
Carbromalum
Cardamomi Semen
Carum
Caryophyllus
Cascara Sagrada
Cataria
Cera Alba
Cera Flava
Cerevisia Fermentum
Cerii Oxalas[1]
Cetaceum
Chloralis Hydras
Chloramina
Chloroformum
Chondrus
Chrysarobinum
Cimicifuga
Cinchona
Cinchonidinæ Sulphas
Cinchoninæ Sulphas
Cinchophenum
Cinnamomum
Cocainæ Hydrochloridum
Coccus
Codeina
Colchicum
Colocynthis
Conium
Copaiba
Coriandrum
Cotarninæ Chloridum
Coumarinum
Creosoti Carbonas
Creosotum
Cresol
Creta Præparata
Crocus
Cubeba
Cupri Sulphas

Delphinium
Dextrinum Album
Dextrosum
Dichloramina
Digitalis

Elaterinum
Emetinæ Hydrochloridum
Ephedrina[1]
Epinephrina
Ergota
Eriodictyon
Eucalyptol
Eucalyptus
Eugenol
Eupatorium
Euresol[1]
Extractum Carnis

Fel Bovis
Ferri Carbonas Saccharatus
Chloridum
et Ammonii Citras
Glycerophosphas
Hydroxidum
Hypophosphis
Lactas
Phosphas Solubilis
Pyrophosphas
Sulphas
Tersulphas
Ferrum
Ferrum Peptonatum
Ferrum Reductum
Formaldehydum

Galla
Gelatinum
Gelsemium
Gentiana
Geranium
Glucosum
Glusidum
Glusidum Solubile
Glycerinum
Glycerylis Nitras
Glycyrrhiza
Gossypium Purificatum
Granatum
Guaiacol
Guaiacois Carbonas
Guaiacum
Guarana

Hexylresorcinol[1]
Homatropinæ Hydrobromidum
Hydrargyri Chloridum Corrosivum
Chloridum Mite
Iodidum Flavum
Iodidum Rubrum
Oxidum Flavum
Oxidum Rubrum
Salicylas
Hydrargyrum Ammoniatum
Hydrastis
Hydrogen Dioxide
Hyoscyamus
Hyoscyaminæ Hydrobromidum

Insulin[1]
Iodoformum
Iodum
Ipecacuanha
Ipomœa

Jalapa
Juniperus

Kaolinum
Krameria

Lactosum
Limonis Cortex
Lobelia
Linum
Lithii Bromidum
Citras
Lupulinum
Lycopodium

Magnesii Carbonas
Chloridum
Citras
Oxidum
Sulphas
Maltum
Malvæ Folia
Mangani Citras
Glycerophosphas
Hypophosphis
Manna
Matricaria
Mel
Mentha Piperita
Mercurochrome[1]
Metaphen[1]
Methenamina
Methylis Salicylas
Morphina and Salts
Myristica
Myrrha

Neoarsphenamina
Neocinchophenum[1]
Nitrogenii Monoxidum
Nux Vomica

Oleum Aethereum
Amygdalæ Amaræ
Amygdalæ Expressum
Anisi
Aurantii
Bergamottæ
Betulæ Empyreumaticum
Cadmium
Cari
Caryophylli
Chaulmoogræ
Chenopodii
Cinnamomi

Coriandri
Eucalypti
Fœniculi
Gossypii Seminis
Juniperi
Lavandulæ
Limonis
Lini
Menthæ Piperitæ
Morrhuæ
Myristicæ
Olivæ
Picis Rectificatum
Pinii Pumilionis
Ricini
Rosmarini
Santali
Sassafras
Sinapis Volatile
Terebinthinæ
Theobromatis
Thymi
Tiglii
Opium
Orthocresol
Oxygenium
Oxyliodide[1]

Pancreatinum
Paraffinum
Paraffinum Chlorinatum
Paraldehydum
Pepsinum
Persio
Petrolatum
Petrolatum Album
Petrolatum Liquefactum
Phenobarbitalum
Phenobarbitalum Sodium[1]
Phenol
Phenolphthaleinum
Phenylis Salicylas
Phytolacca
Phosphorus
Physostigmina and Salts
Pilocarpinæ Hydrochloridum
Pinus Alba
Pituitarium
Pix Carbonis
Pix Pini
Plumbi Acetas
Monoxidum
Oleas
Podophyllum
Populi Gemmi
Potassa Sulphurata
Potassii Acetas
Bicarbonas
Bitartras
Bromidum
Carbonas
Chloras
Citras
Guaiacol Sulphonas[1]
Hydroxidum
Hypophosphis
Iodidum
Permanganas
et Sodii Tartras
Procaina
Prunus Virginiana
Pyrogallol
Pyroxylinum

Quassia
Quercus
Quillaia
Quinina and Salts
Quinidinæ Sulphas

Renninum
Resorcinol
Rheum
Rhus Glabra
Rubi Idæi Fructus

Salicinum
Sanguinaria
Santalum Rubrum
Santalum Album
Santoninum
Sapo
Sapo Mollis
Sarsaparilla
Sassafras
Scilla
Scoparius
Scopolaminæ Hydrobromidum
Senega
Senna
Serpentaria
Sevum
Sinapis Nigra
Sodii Acetas
Benzoas
Bicarbonas
Biphosphas
Boras
Bromidum
Cacodylas
Carbonas
Chloridum
Citras
Glycerophosphas
Hydroxidum
Hypophosphis
Indigotindisulphonas
Iodidum
Nitris
Perboras
Phosphas
Salicylas
Sulphas
Thiosulphas
Sparteinæ Sulphas[1]
Spiritus Frumenti
Spiritus Vini Vitis
Stillingia
Stramonium
Strontii Bromidum[1]
Salicylas
Strophanthus
Strophanthinum
Strychnina
Styrax
Sucrosum
Sulphonethylmethanum
Sulphur
Sumbul

Talcum
Taraxacum
Terebene
Terebinthina
Terpini Hydras
Terra Silicea Purificata
Theobromina
Theophyllina
Thymol
Thymolis Iodidum
Thymus
Thyroideum
Tolu
Tolysin[1]
Tragacantha
Trinitrophenol
Triticum

Ulmus
Uva Ursi

Vaccinum Vario'æ
Valeriana
Vanilla
Vanillinum
Veratrina
Veratrum Viride
Viosterol[1]

Yohimbine[1]

Zinci Oxidum
Phosphidum[1]
Stearas
Sulphas
Zingiber

When should our students begin to specialize is a question that will probably never be settled to the entire satisfaction of all teachers in colleges of pharmacy. The following discussion by Dr. George D. Beal is enlightening because it presents a similar problem from the standpoint of the employer of college graduates. His arguments and illustrations are convincing and his paper deserves careful study.—C. B. JORDAN, *Editor*.

CHEMICAL EDUCATION AND INDUSTRIAL RESEARCH.

BY GEORGE D. BEAL.[1]

In accepting the invitation to prepare a paper for the Chemistry Teachers' Conference, I did not realize at the time that my words were to be a formal opening to a symposium on Chemical Education and Industrial Research. However, at the Baltimore meeting of this section I had the privilege of speaking on the teaching of analytical chemistry, when I presented some ideas similar to those which I intend to advance to-day. My laboratory schedule did not meet with the approval of some who discussed that paper, so that I am glad to have this opportunity of restating my position, this time in connection with what some may regard as a higher plane of endeavor.

Thinking back over two years, I recall that our divergence of opinion came over the question of the content of a laboratory course in analytical chemistry. It has been my experience in teaching this subject that the ideal course, as in organic or physical chemistry, is one that is based upon typical operations and reactions, rather than one which empirically goes through a series of experiments chosen merely because they represent determinations that may be made by the student if he later chances to enter a control laboratory.

If every student upon entering college was so omniscient that he could accurately and adequately foretell his professional future, his curriculum might be arranged to fit his future needs. Think of the medley of courses we would then find described in our catalogs, and of the predicament of the instructor who was required to correlate the grades because of the requirements imposed by regulatory and licensing boards. Since we have not the gift of prophecy, and must for administrative purposes have some uniformity of requirement and performance, any curriculum and any course therein must be based upon that parable of the house that was builded upon a rock, which because of the strength of its foundation could not fall.

One of my early duties in the teaching profession was to give instruction in quantitative analysis to a large class of agricultural students. Many of them objected strenuously to spending their time on the determination of simple radicals such as chloride and sulphate in salt mixtures and the titration of samples of organic acids and soda ash. It would be so much better, they reasoned, to substitute samples of soil and fertilizer for these simple things and thus quickly obtain precious practical experience. It was only when they came close to the end of the semester and took up the more complete analysis of limestone and rock phosphates that they realized the effect of a lack of experience and technic.

As a result of their constant complaint I finally took my problem to the professor in charge of the work in soil fertility, for which my course was prerequisite.

[1] Assistant Director, Mellon Institute of Industrial Research.

This gentleman, an authority whose fame was world-wide, was good enough to sympathize with me in my dilemma, but asked me to continue just as I was doing. His words were in substance:

> "These students must come to us with the ability to weigh, to filter and to titrate. They must understand the theories of chemical calculations and therefore must know the reactions that govern analytical procedures. We can give them outlines for the analysis of soils and fertilizers, but we cannot in the time allotted us teach them those fundamental things that will enable them to plan, execute and interpret the analyses of agricultural materials."

Just as there are both empirical and systematic methods of conducting chemical analyses, so are there empirical and systematic methods of research. The chemical monographs of the Pharmacopœia are empirical, because experience has shown the character of the adulterations that may be expected and has also dictated the simplest means of dealing with them. But the analysis of a proprietary by a purely empirical series of procedures is liable to require an indefinite time unless the operator is guided by some knowledge of probable composition, which means experience or fundamental training.

With these two general methods for the conduct of research, there is a vast series of blends with almost infinitesimal shadings. At one end of the series is that method of attack known as the "try every bottle on the shelf." At the other end is patient, systematic investigation, in which every ramification is followed to its logical conclusion. Probably the research genius is the person who, following a systematic program, best recognizes the time to apply empiricism, or, as expressed by many, to "play his hunch."

There is no doubt but that both brilliant and valuable discoveries have been made in an empirical fashion. Would you, however, as hard headed business men, be willing to entrust the development of what might eventually become one of your most valued possessions to the hands of a man whose sole recommendation was a reputation as a lucky guesser?

It would be bigotry on my part to maintain that ability to carry on any one type of research does not depend upon specific training. The man who is to effect the most profound synthesis of a new medicinal agent must admittedly be best versed in organic chemistry, and some one well trained in biochemistry will probably have most to do with the isolation of a hormone. Therefore you will say that we must include specialization in organic and physiological chemistry in the training of research chemists. But some of the very important studies now required in pharmacy are of a physicochemical nature, and the Pharmacopœia still includes a lengthy list of inorganic chemicals, while organo-metallic compounds, that meeting-ground of the two great sub-divisions, are growing rapidly in importance.

In the writer's opinion industrial pharmacy, just like industrial chemistry, will be a constantly changing profession, with new interests and new problems coming to light at frequent intervals. If therefore we have a wealth of men of a high degree of specialization in one field, and the fashion of manufacturing pharmacy changes, those specialists who cannot change with the fashion will be doomed to great disappointment.

If a man must be an organic chemist this year and an inorganic chemist next, his chances of success will be strongest if he is first of all a chemist, and afterward a

specialist. Very few students complete a curriculum without showing a relatively superior sort of proficiency, or interest, in one division over another. This, carried on into graduate study, or practical research, eventually produces the specialist. But even the specialist is of little real value if his specialty is developed at the expense of his collateral training.

We are asked frequently in our organization which division of chemical science is most profitable for specialization. We have to reply that strong fundamental training and adaptability are probably the two most important requirements. The reason for this is that we cannot accurately predict a year ahead, even in good times, what the need for research workers will be. Our needs may be, and doubtless are, different from those of a manufacturing house, but the latter is confronted with changing economic conditions just as we have been, and quick shifts of front are undoubtedly required to meet new needs or competitions.

During the past week we have learned of the experience of an eighty-year-old industrial house which has normally maintained a large and efficient research staff and which even to-day is operating to a practically normal extent. Last fall they were obliged in a general move of economy, due partly to a fear for the future, to reduce their staff 25 per cent. Notwithstanding this apparently serious reduction, they tell us that the volume of work produced has not appreciably minimized. According to the statement of one of their executives, more work is actually being done by the reduced staff than by the full staff previously. The mediocrists of the staff have been eliminated, with their hindrances to the more brilliant members, and the men remaining are working more efficiently and intensively.

In determining the personnel of the residual research force, the important criterion has been researchfulness. Proof of this is the demonstration of power by contribution or by publication. By this I make no reference to the publication by a student of a thesis or dissertation, for the reason that in nearly every such instance the idea and the spirit of the work, and oftentimes a large part of the actual content of the contribution, is the work of another and older person. Only such as can be a witness of independent thought can be considered an index of researchfulness, and no man's work as a researcher has been demonstrated until he has complied with these criteria.

Let us conclude then that intense specialization should be a sign of interest rather than of limitation, and that it will be built upon a sound foundation of general knowledge. After all, specialization on the part of the well-grounded person is no limitation to his usefulness or progress. I have mentioned on other occasions my first actual teaching connection in a university department of chemistry. There, in a well-rounded department, with eighteen members of the staff of doctorate standing, nine of them had obtained their highest degree in organic chemistry, although they were teaching and directing research as well in inorganic, analytical, industrial and sanitary chemistry. Two other examples that have been mentioned on other occasions are those of two of the three student founders of the now national honorary chemical society. One of these men, majoring in fuel chemistry, became one of the country's leading biochemists, while the other, equally determined to specialize in animal nutrition, became a fuel expert of national renown.

Furthermore, success in the field of research depends upon far more than the actual training received. Industrial research requires, on the part of some in the

higher places, at least, a sense of economic values; it requires a knowledge of what has been and is being done on the other side of the fence; it requires an ability to work and to think; it requires also an imaginative spirit and an argumentive spirit, and many times one which will take nothing for granted. Just as there are some chemists who fit into an analytical laboratory not because they are useless elsewhere but because they have a mysterious quantitative sense that the average chemist lacks, so there are also chemists who have all of those qualities that go to make the ideal research man, yet apparently lack the brilliance of some of their laboratory colleagues. Some of the soundest thinkers continue to plod, because they never get beyond the immediate problem to see the subject in its broadest relations. Others have what on first sight appears to be a lucky touch, but later turns out to be native ability, plus sound basic training, plus the inspiring examples of teachers who had a respect for things around them.

There have been many defects in pharmaceutical education in the past. Some of these are due to bias and bigotry on the part of teachers who have been regarded as leaders in the profession. It seems that in schools connected with the art of healing, including medicine, dentistry and pharmacy, there has been a greater tendency toward inbreeding in the faculties than is observed in other scientific and technical faculties. There are few faculties in pharmacy that have brought in new members from outside their own walls, who can introduce new methods of teaching and help break down conservatism and tradition.

Chemical education in the two-year course in pharmacy could not produce trained chemists. Such training in the short courses should be limited to what is actually necessary for the handling of chemical substances used in the compounding of prescriptions. The purpose of the four-year course, however, is to provide the pharmacist with a more substantial education, in which the ground work for practicing the art of pharmacy is to be reinforced with instruction in collateral branches, and at the same time backed by a more substantial preparation for the world of business and for one's proper place in community life.

The organization of a substantial four-year course in pharmacy will not be accomplished by a mere extension of the hours in each course or a multiplication of experiments in laboratory courses. New subject matter must be added to curriculums and courses, and this must be carefully considered in the light of more adequate preparation for subsequent courses. Above all, the introduction of topics and courses must be for more substantial reasons than the dictates of educational fashions and fads.

It is out of place in this paper to discuss the value of individual topics and courses in an educational program. There are two matters that may be stressed, however. One of these is the proper place of the study of economics in relation to chemistry and pharmacy. The literature in this field is ample, and the importance of the subject to any student planning to make industrial research his life work is unquestioned.

The other is the place of the library in education and research. The study of the use of chemical literature has been a development of the last twenty years in schools of chemistry, due largely to the pioneering work of the late Miss Sparks at Illinois and Mellon at Purdue. The AMERICAN PHARMACEUTICAL ASSOCIATION is one scientific society that has insisted from the beginning on the preservation of

research records through the "Report on the Progress of Pharmacy." Instruction in bibliochresis should be made a part of every curriculum in pharmacy. The college library should not be considered as a show place, but as a work room for every student in which he is taught how to use the valuable reports of workers in this and collateral fields.

Some schools with rich equipment and teachers individually of national note will continue to turn out students of mediocre grade, while others, sometimes apparently less favored will furnish leaders to the profession the country over. Such school spirits are not created over night by a board of trustees, but come from the inspiration of one man or a group of kindred spirits who keep their students welded into such a body that men separated in school by ten or more years feel instantly called to each other. The work and spirit of the school as a whole determine whether its educational pattern is one that leads to research success in pure science or in industry.

August 13, 1932.

COMMITTEE REPORTS

A PROPOSED STANDARD TABLE OF POISONS.*

Because of the impossibility of framing a definition for poison which will serve as an accurate guide in every case, and also because of the unsatisfactory condition of many state poison laws, The National Drug Trade Conference has undertaken the preparation of a reference list of drugs and chemicals which should properly bear the poison label when dispensed otherwise than upon the prescriptions of physicians.

The tentative list presented in the following pages is admittedly imperfect, and is submitted with the express purpose of eliciting comment and criticism.

Suggestions are desired as to the addition of agents not included in the list, the exclusion of some which are now included, criticism of the various degrees of concentration proposed, or comments regarding any other phase of the subject.

After revision, with the aid of the comments which are expected to be received, copies of the revised list will be presented to all of those who have responded to this request.

Comments may be sent to the secretary of The National Drug Trade Conference,

E. F. KELLY,
10 West Chase Street, Baltimore.

NEED FOR A STANDARD LIST OF SUBSTANCES TO BEAR POISON LABEL.

The need for a generally accepted, or "standard" list of substances which should bear a poison label when dispensed is found in the fact that it is practically impossible to propose a definition of poison that will serve as a sufficient guide under all circumstances. The following attempted definitions from various authorities will make this evident.

Standard Dictionary.—"Any substance that when taken into the system acts in a noxious manner by means not mechanical, tending to cause death or serious injury to health."

Webster's New International Dictionary.—"Any agent which, introduced into the animal organism, may produce a morbid, noxious or deadly effect."

Bouvier's Law Dictionary.—"A substance of definite chemical composition, which when taken into the living organism is capable of causing impairment or cessation of function."

The Encyclopedia of Law.—"Any substance which when taken, applied to the body ex-

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* Report of the Committee on Potent and Toxic Drugs of The National Drug Trade Conference.

ternally or in any way introduced into the system, is capable, without acting mechanically, but by its own inherent qualities, of destroying life."

All of the above and dozens of other definitions which might be cited are constructed upon the theory that drugs and chemical compounds can be divided into those which are distinctly poisonous and those which are distinctly non-poisonous. Unfortunately this is not true, and there is scarcely a known substance soluble in the body fluids which will not under certain circumstances "cause death or serious injury to health," or which may not "produce a morbid, noxious or deadly effect."

Dosage is always a controlling element. The same substance may be a useful food stuff, a comparatively harmless medicine or a toxic agent according to the amount taken into the body at one time. The method of ingestion is likewise of importance, since numerous substances harmless when taken into the stomach may react dangerously when inhaled, or when injected directly into the circulation.

To consider all such substances poisons would require the placing of a poison label upon such common articles as table salt, vinegar, pepper, mustard, capsicum, cloves, epsom and Glauber salts, quinine sulphate and a host of other commonly used articles that, under ordinary circumstances are harmless, but which in excessive amounts or when improperly used may occasion serious injury or even death.

To meet the troublesome matter it is sometimes attempted by statute to define a poison by specifying the dangerous or toxic dose. Thus a Pennsylvania statute prescribes that a poison, "shall be any drug, chemical or preparation which, according to standard works on medicine or materia medica, is liable to be destructive to adult human life in quantities of sixty grains or less."

Some objections to such a definition are:

1. That it does not specify what shall be considered "standard works on medicine or materia medica."

2. That numerous works which might properly be considered as standard authorities frequently do not state the toxic doses of many of the substances of which they treat.

3. That there is frequently wide variation in the toxic doses of the same substances as stated in works by different authors.

4. That many dangerously toxic substances used in the arts are not described in works on medicine and materia medica.

USE OF INDEFINITE GENERAL TERMS OBJECTIONABLE.

Occasionally a poison label statute, after designating a list of substances to have the poison label, concludes with some indefinite general phrase such as "all other poisonous alkaloids and their salts," "all other virulent poisons," "all other substances belonging to the class commonly known as poisons," or other similar phraseology. Such indefinite general terms are objectionable, since, as we have seen, nearly all drugs and medicines are capable of acting poisonously in excessive doses or under certain conditions.

Since it is apparently impossible to devise general definitions to serve as a safe guide in the labeling of poisons, the only alternative seems to be the preparation of a list of substances which, in the opinion of experienced pharmacists, pharmacologists and physicians should bear the poison label when dispensed otherwise than upon the prescriptions of qualified physicians.

Such an attempt is presented in the following pages. It should be kept in mind that the list submitted is to be regarded as provisional or tentative, and is proposed with the object of calling forth suggestions for its improvement.

GENERAL PRINCIPLES.

In the opinion of the committee the following general principles should prevail in the selection of a list of the agents which should bear the poison label, and also of the conditions under which such label may with safety be omitted.

Public Interest Must Govern.—The sole purpose of the poison label is to protect the public health from injury through the improper use of toxic drugs, either by misadventure or criminal design, and to such public purpose all other interests must yield, regardless of trade customs or usages to the contrary.

Warning of Poison Label Should Not Be Weakened by Excessive Use.—The warning effect of the poison label should not be weakened by promiscuous use upon any and all substances which may prove injurious when taken in excessive quantities. If, for example, the poison label were to be placed upon common salt, nutmeg, black pepper, etc., which have been known to produce fatal results in excessive quantities, its warning effect would be gradually weakened until it would cease to be effective when used upon such truly dangerous substances as phenol and mercury bichloride. Such a lessening of the effectiveness of the poison label obviously would not be for the public benefit, and the use of the poison label should, therefore, be confined to cases where a warning of the dangerous character of the substance will serve a really useful and necessary purpose.

Simple and Compounded Drugs and Chemicals.—Toxic drugs and chemicals dispensed in undiluted form may be in a different category than when compounded with other and non-toxic ingredients. While it is clear that a salt of strychnine dispensed as such should always bear the poison label, it would obviously be absurd to require such label upon Elixir of Iron, Quinine and Strychnine, in which the percentage of the stronger alkaloid is so low as to make the toxic qualities of the preparation negligible.

It follows, therefore, that compound preparations should bear the poison label only when the content of toxic drug is in such proportion as to render the combination dangerous as such.

REGISTRATION OF SALE AND USE OF RED LABEL.

Numerous poison label statutes divide their included agents into two schedules, A and B, according to their toxicity. In such case it is customary to require registration of the sale of the agents included in the more toxic schedule, or which are especially liable to be used for criminal purposes. Sometimes also, it is required that the labels of such agents be printed or written in red ink.

In the following table the red label is indicated for the more toxic substances, and the registration of sale for those most likely to be employed as homicidal agents or for other unlawful use, as abortifacients, though all are included in a single alphabetical list.

Drugs Dispensed on the Prescriptions of Physicians and Dentists.—Drugs and medicines dispensed on the prescriptions of physicians or dentists should not bear the poison label, unless the prescriber shall expressly direct that such label be attached.

Preparations dispensed as prescriptions intended for external use only but which might act harmfully if taken internally, may be labeled "for external use," "not to be taken internally," or with some equivalent language to emphasize their purpose for external application.

Preparations Dispensed on Veterinarian Prescriptions.—Preparations dispensed on the prescriptions of legally qualified veterinary physicians, and which might produce harmful results if administered to human patients, should be labeled either "not for human use," or "for veterinary use only."

Character of the Poison Label.—To accomplish its purpose the word POISON should be conspicuous, and hence should not be made obscure through the use of ornamental type or by being printed on a confusing background.

The size of type will to some extent be governed by the size of the label, but it should always be large enough to be perfectly distinct.

For these reasons the word POISON should be printed in uncondensed gothic capital letters, preferably larger than, but at least as large as any other letters on the label, and should be printed on a plain back-ground in ink of distinctly contrasting color.

To distinguish between moderately poisonous agents and those which should be regarded as especially dangerous, the labels of the latter should be printed in red ink. The names of such substances are indicated in the accompanying table.

In emergency when printed labels are not available, written labels should correspond to the same rules as to relative size of letters and color of ink.

The names of antidotes and the antidotal measures should appear immediately under the word POISON, and should be plainly legible.

The following is a form of poison label which has been approved by the department of the Federal Government which has in charge the administration of the Federal Caustic Poisons Act.

NITRIC ACID

POISON

ANTIDOTES:—INTERNAL—Drink a teaspoonful or more of Magnesia, Chalk, Whiting or Wall Plaster, or small pieces of Soap softened with water, in Milk, Mucilage or White of Raw Eggs.
EXTERNAL—Wipe off the acid gently, immediately flood the surface with water, using soap freely, then cover with moist Magnesia or Baking Soda. **Call a Doctor.**

PROPOSED TABLE OF DRUGS, CHEMICALS AND PREPARATIONS WHICH SHOULD BE DISPENSED WITH THE POISON LABEL.

In keeping with the above provisions, and except as otherwise noted, the following drugs, chemicals and preparations should bear the poison label:

1. When not dispensed in pursuance of the prescriptions of physicians, dentists or veterinarians.

2. When dispensed in the undiluted or uncompounded condition, or if compounded, when the degree of concentration of the toxic ingredients equals or exceeds the limit of concentration specified in the table.

Acetone: In concentration of 10%. Red label.

Acid: Carbolic, see Phenol.

Acids: Hydrocyanic, hydrofluoric and hydrosilicofluoric in all concentrations. Red label. Sales to be registered.

Glacial, mono-, di- and trichloracetic acids, and anhydride, hydrochloric, hypochlorous, hydrobromic, hypophosphorous, phosphoric (glacial or metaphosphoric, orthophosphoric), oxalic and sulphuric, in concentrations of 10%.

Picric and nitric, in concentrations of 5%.

Aconite: Root, leaves and all preparations, and aconitine, in all concentrations. Red label. Sales to be registered.

Alcohol, Ethyl: When denatured with wood alcohol, in concentration of 20%.

Amylic: In concentration of 5%.

Methyl or Wood: In concentration of 10%. Red label.

Alkaloids and Salts:

Aconitine, in all concentrations.
Atropine, in all concentrations.
Brucine, in concentration of $^1/_{10}$%.
Cocaine, governed by Federal Anti-Narcotic Law. See Coca Leaves.
Codeine. See opium alkaloids.
Colchicine, in concentration of 1%.
Coniine, in concentration of $^1/_{10}$%.
Daturine, in concentration of $^1/_{10}$%.
Delphinine (staphisagrine), in concentration of $^1/_{10}$%.
Dionine. See opium alkaloids.
Gelseminine, in concentration of 1%.
Hyoscine, in all concentrations.
Hyoscyamine, in all concentrations.
Lobeline, in all concentrations.
Morphine. See opium alkaloids.
Opium alkaloids, salts and compounds. Sale governed by Federal Anti-Narcotic Law. Should be dispensed only on prescription.

Narceine. See opium alkaloids.
Narcotine. See opium alkaloids.
Nicotine, in concentrations of 1%.
Physostigmine, in concentration of $^1/_{10}$%.
Sabadine, in concentration of $^1/_{10}$%.
Scopolamine, in concentration of $^1/_{10}$%.
Sparteine, in concentration of 1%.
Staphisagrine. See Delphinine.
Strychnine, in concentration of $^1/_{10}$%.
Thebaine. See opium alkaloids.
Veratrine, in concentration of $^1/_{10}$%.

Ammonium: Hydroxide, chromate, dichromate, fluoride, oxalate, picrate, in concentrations of 5%.

Amyl Nitrite: In all concentrations. Red label.

Aniline Oil: In all concentrations. Red label.

Antimony: All compounds including tartar emetic in concentration of 5%, except sulphide.

Apomorphine: Sale governed by Federal Narcotic Act.

Arsenates and *Arsenites:* In concentrations of 1%. Red label.

Arsenic: Metallic or elemental, and all compounds and preparations, in concentrations of 1%. Red label. Sales to be registered.

Arsphenamine: Should be dispensed only on prescription.

Ascaridol: Should be dispensed only on prescription.

Atropin (resinoid) and *Atropine* (alkaloid): Should be dispensed only on prescription.

Barium: All salts, compounds and preparations except barium sulphate.

CAUTION: Barium sulphate should not be confused with the *sulphide*, which is very poisonous when taken internally. The names of these should *not* be abbreviated on labels or in prescriptions.

Belladonna: Leaves, root and all compounds and preparations, atropin (resinoid) and atropine and its salts in all concentrations. Red label.

Benzaldehyde: Natural or synthetic, in concentration of 2%. Red label.

Benzene or Benzol: In concentration of 10%.

Bromine: Elemental or liquid, and chloride, in concentrations of 2%.

Bromoform: In concentration of 10%.

Brucine: In concentration of $^1/_{10}$%. Red label.

Cacodylates: In all concentrations. Red label.

Calabar Bean: See Physostigma.

Calcium: Arsenate and arsenite, in concentrations of 1%. Red label.

Cannabis: Crude drug and all preparations in concentrations of 10%.

Cantharides: Powder, and all preparations in concentrations of 2%. Red label. Sales to be registered.

Carbon Disulphide: In concentration of 5%.

Carbon Tetrachloride: In concentration of 10%.

Chloral Hydrate: In concentration of 10%. Should be dispensed only on prescription.

Chloroform: In concentration of 10%.

Chromium: All salts, compounds and preparations, in concentrations of 5% and over.

Cobalt: All salts, compounds and preparations in concentrations of 5%.

Coca: Coca leaves, cocaine, salts and derivatives—sales governed by Federal Anti-Narcotic Law. Should be dispensed only on prescription.

Cocaine: See Coca.

Cocculus Indicus or Fish-berry: Crude drug and preparations, and picrotoxin in all concentrations. Red label. Sales to be registered.

Codeine: Governed by Federal Anti-Narcotic Law. Should be dispensed only on prescription.

Colchicum: Corm and preparations in concentrations of 5%. Colchicine, in concentration of 1%. Red label.

Collodium: Blistering, cantharidal, in all concentrations.

Coniine: See Conium.

Conium: Fruit, leaves and all preparations in concentrations of 5%. Coniine and salts in concentration of 1/10%. Red label.

Copper: All salts, compounds and preparations, in concentrations of 5%, *except* oleate, oxide, palmitate, phosphate, resinate, selenate, silicofluoride, stearate and sulphide.

Creosote: From wood or coal tar, in concentrations of 10%. Red label.

Cresol: Cresol and creolin, in concentrations of 10%.

Croton: Seeds, croton oil and crotin in concentrations of 1%. Red label. Sales to be registered.

Curare: Crude drug, derivatives and preparations in all concentrations. Red label. Should be dispensed only on prescription.

Cyanides: In all concentrations. Red label. Sales to be registered.

Datura: Seeds, leaves and preparations in concentrations of 5%. Daturine and salts in concentrations of 1/10%. Red label. See also Stramonium.

Delphinine: See Staphisagria.

Derris and Rotenone: In concentrations of 5%.

Digitalis: Leaves and all compounds and preparations in concentrations of 5%. Digitalein and digitalin in concentrations of 1%. Red label.

Dionin: Sales governed by Federal Anti-Narcotic Law. Should be dispensed only on prescription.

Dover's Powder: Sales governed by Federal Anti-Narcotic Law. Should be dispensed only on prescription.

Ether, Ethyl: In concentration of 10%.

Ethyl Chloride: In concentration of 5%. Red label.

Ethyl Cyanide: In all concentrations. Red label. Sales to be registered.

Euphorbium: Gum resin and preparations in concentrations of 10%.

Fluorides: When soluble in water, in concentrations of 5%. Red label.

Formaldehyde: In concentrations of 5%.

Gamboge: In concentration of 5%.

Gelsemium: Root and preparations, in concentrations of 5%. Alkaloids and salts in concentrations of 1%. Red label.

Hellebore: Black, White, Green, and preparations in concentrations of 5%. Red label.

Homatropine and Salts: In concentrations of 1%. Red label.

Hyoscyamus: Leaves, root and preparations in concentrations of 5%. Hyoscyamine, hyoscine and salts in all concentrations. Red label.

Ignatia: Bean and preparations in concentration of 5%. Red label.

Iodine: Elemental or metallic, mono- and tribromide, mono- and trichloride and preparations, in concentrations of 2%. Red label.

Larkspur: Seed and preparations in concentrations of 5%. Red label.

Lead: All salts, compounds and preparations, in all concentrations except pigments ground in oil. Red label.

Lobelia: Herb and preparations in concentrations of 5%. Lobeline and salts in all concentrations. Red label.

Mercury: All salts, compounds and preparations in concentrations of 1%. Red label. Sales of bichloride and nitrate to be registered. *Exceptions:* metallic mercury, calomel, black and red sulphides, mercury with chalk, mass of mercury.

Methyl Alcohol: In concentration of 10%. Red label.

Mezereum: Bark and preparations, in concentrations of 10%.

Morphine, Alkaloid and Salts: Sale governed by Federal Anti-Narcotic Law. Should be dispensed only on prescription.

Narceine and Narcotine: Sale governed by Federal Anti-Narcotic Law. Should be dispensed only on prescription.

Neoarsphenamine: Should be dispensed only on prescription.

Nicotine: Alkaloid and all salts and solutions in concentrations of 1%. Red label.

Nitrobenzene (Oil of Mirbane): In concentrations of 5%. Red label.

Nux Vomica: Crude drug and preparations in concentrations of 1%. Strychnine and salts, brucine and salts, in concentrations of 1/10%. Red label. Sales to be registered.

Oil of Bitter Almond: Natural or artificial, in concentrations of 2%. Red label. Sales to be registered.

Croton: In concentration of 1% and over. Red label. Sales to be registered.

Mustard, Artificial: In concentration of 1%. Red label. Sales to be registered.

Pennyroyal: In concentrations of 5%. Red label. Sales to be registered.

Savin: In concentration of 5%. Red label. Sales to be registered.

Tansy: In concentration of 5%. Red label. Sales to be registered.

Opium: Crude drug, all derivatives, preparations, alkaloids and salts. Sale governed by Federal Anti-Narcotic Law. Should be dispensed only on prescription.

Paraldehyde: In concentration of 5%.

Phenol (Carbolic Acid): In concentration of 5%. Red label. Sales to be registered.

Phosphorus, Yellow, and *Phosphides:* In all concentrations. Red label.

Physostigma (Calabar Bean): Crude drug and all preparations, in concentrations of 2%. Physostigmine and salts, in concentration of $^1/_{10}$% and over. Red label. Sales to be registered.

Phytolacca: Crude drug and preparations, in concentrations of 10%.

Picrotoxin: See Cocculus.

Poke Root: See Phytolacca.

Potassium: Chromate and dichromate, ferricyanide (red prussiate), ferrocyanide (yellow prussiate) oxalates—acid, neutral and tetroxalate, permanganate, sulphocyanate, tartar emetic, in concentrations of 10%. Red label.

Arsenate and arsenite, in concentrations of 1%.

Cyanide in all concentrations. Red label. Sales to be registered.

NOTE: Potassium ferrocyanide, (yellow prussiate) is said to be non-poisonous when pure, but as it may release hydrocyanic acid when in contact with other acids it should bear a poison label.

Potassium Carbonate: In concentrations of 10%.

Hydroxide or *Hydrate:* In concentration of 5%.

Pyrogallol, Pyrogallic Acid: In concentration of 5%.

Rhus Toxicodendron: Crude drug and preparations in concentrations of 1%. Red label.

Sabadilla, Cevadilla: Drug and preparations in concentrations of 5%.

Sabadine: Alkaloid and salts in concentrations of $^1/_{10}$%. Red label. Sales to be registered.

Scopola: Drug and preparations in concentrations of 5%. Scopolamine and salts in concentrations of $^1/_{10}$%. Red label.

Silver: Arsenite, nitrate, sulphate, in concentrations of 1%. Red label.

Sodium: Arsenate, arsenite, carbolate, chromate, dichromate, ferricyanide, fluoride, oxalate, sulphocyanate, in concentrations of 1% and over. Cyanide, in all concentrations. Red label.

Sodium: Metallic and sodium amalgam, hydroxide, hydrate or caustic soda, ethylate, sulphide, in concentrations of 5% and over. Red label.

Solanum: Drug and preparations in concentrations of 5%. Red label.

Sparteine: Alkaloid and salts in concentrations of 1%. Red label.

Spirit of Nitroglycerin (Glonoin): In concentration of 1%. Red label.

Spirit of Phosphorus: In concentration of 1%. Red label.

Squill: Drug and preparations in concentrations of 10%.

Staphisagria: Crude drug and preparations in concentrations of 5%. Delphinine or staphisagrine in concentrations of $^1/_{10}$%. Red label.

Stramonium: Crude drug and preparations in concentrations of 5%. Red label.

Strophanthus: Crude drug and preparations in concentrations of 5%. Strophanthine and salts in concentrations of $^1/_{10}$%. Red label. Sales to be registered.

Strychnine: All salts and compounds in concentrations of $^1/_{10}$%. See also Nux Vomica. Red label. Sales to be registered.

Tansy: Volatile Oil, in concentration of 5%. Red label. Sales to be registered.

Tetrachloroethylene: In concentration of 10%.

Thallium: Acetate, chloride, hydroxide, nitrate, sulphate, in concentrations of 1%. Red label.

Thebaine: Sale governed by Federal Anti-Narcotic Law. Should be dispensed only on prescription.

Tin: Stannous and stannic bromides and chlorides in concentrations of 5%. Red label.
Trinitrophenol: See Picric Acid.
Uranium: Acetate, nitrate, sulphate, in concentrations of 5%. Red label.
Veratrine: Alkaloid and salts in concentration of 1%.
Veratrum Viride: Drug and preparations in concentrations of 5%. Red label.
Water, Ammonia: In concentration of 5%. Red label.
Zinc: Acetate, bromide, chloride, nitrate, sulphate, in concentrations of 5%. Red label.

Respectfully submitted,

Committee on Potent and Toxic Drugs.
A. G. DuMez
S. L. Hilton
Robt. L. Swain
A. C. Taylor
J. H. Beal, *Chairman.*

NATIONAL CONFERENCE ON PHARMACEUTICAL RESEARCH.—COMMITTEE NO. 1.

PHARMACEUTICAL DISPENSING.

REPORT FOR YEAR ENDED MAY 31, 1932.

BY WILLIAM J. HUSA, CHAIRMAN.

During the year a number of interesting and valuable contributions dealing with various phases of dispensing pharmacy have appeared in the literature.

Opthalmic Ointments.—In a recent English article (1) the preparation of opthalmic ointments containing alkaloids or alkaloidal salts was discussed. These are usually made by one of four different methods, each of which has some advantages and some disadvantages. In the first method, the free alkaloid is dissolved directly in the fatty base with aid of heat. The disadvantage of this method arises from the use of heat, which may decompose the alkaloid or form a saturated solution at a higher temperature which will crystallize on cooling. The second method involves the preparation of a neutral alkaloidal oleate, which is then mixed with the fatty base. Here again the heat used in making the oleate may cause decomposition. In the third method, a readily soluble alkaloidal salt is dissolved in a very small quantity of water and this solution is incorporated in the base. The chief disadvantage of this process is that water may evaporate from the ointment on standing, with formation of crystals of the alkaloidal salt. In the fourth method the finely powdered alkaloidal salt is mixed with the ointment base; by this method it is difficult to obtain an ointment that is really as free from gritty particles as would be desired.

The method proposed for the new British Pharmacopœia involves the use of a base composed of equal parts of yellow soft paraffin and wool fat, the mixed fats being filtered while hot and then sterilized at 150° C. for one hour. The alkaloidal salt is dissolved in the smallest possible quantity of distilled water, the melted base is added and the mixture triturated until cold.

Lascoff (2) suggested that an opthalmic prescription calling for 5% of argyrol in vaseline should be filled by dissolving the argyrol in the minimum amount of water, taking this up with a small amount of lanolin and incorporating in the vaseline.

Insolubility of Pills.—In a French journal, Henri Griffon (3) reported that a person swallowed 100 granules, each containing 1 mg. of strychnine sulphate; after 3 hours, 25 granules were recovered intact by washing the stomach, along with 15 partially disintegrated granules. Similar reports have appeared at various times, indicating that sometimes pills and tablets will not dissolve or disintegrate due to some defect in the coating or method of manufacture, or due to hardening on long storage. Griffon recommends that tests be made in artificial gastric and pancreatic juices to determine whether or not disintegration takes place.

In this connection, two Danish pharmacists have reported (4) that pills or tablets made with agar-agar disintegrate more quickly than with other excipients. In this case dilute alcohol is used as a moistening agent.

Enteric Coating of Capsules.—The enteric coating of capsules appears to have received more attention recently in this country than in others. S. L. Hilton (5) has recommended coating with shellac, using a solution of white shellac in Spirit of Ammonia, U. S. P. VIII, followed by a coating of salol.

T. J. Bowers (6) recommends that the capsules be coated by spraying with melted salol, using a straight stem medicinal atomizer. One person shakes the capsules in a glass mortar while another sprays on the salol. Bowers states that after a little practice, 100 or more capsules can be coated in less than two minutes. He also states that the salol sticks to the capsules like glue. We have tested this method at the University of Florida and have found the method very convenient and rapid, but the salol soon becomes crystalline and fails to adhere sufficiently.

For making keratin-coated capsules, Lascoff recommends (7) that the capsules first be coated with an alcoholic solution of shellac in order to harden the capsule and present a suitable surface for the keratin. The keratin, dissolved in stronger ammonia water, is then applied. The coated capsules are inserted in empty capsules of the next larger size.

Incompatibilities.—The incompatibilities of silver protein compounds were discussed in an article published in England (8). It was stated that silver protein compounds are liable to precipitate alkaloids from solutions of their salts on account of the alkalinity, which is variable even in different samples of the same product. A 10% solution of argyrol gave a precipitate with very small quantities of cocaine hydrochloride, but was compatible with comparatively high proportions of cocaine nitrate. No incompatibility was observed in solutions containing 2% of cocaine hydrochloride and 10% of protargol, silver nucleinate or a non-proprietary brand of silver-vitellin. It was concluded that owing to the variations in the silver protein compounds it is inadvisable to mix them with cocaine salts, but if the alkaloid is necessary it should be used in the form of the nitrate.

In a Swiss journal, J. B. Lang reported (9) that an ointment consisting of cold cream with 2% of mercuric chloride becomes red, due to precipitation of basic mercuric chloride due to alkalinity of the borax present in the cold cream. This was prevented by addition of an amount of boric acid equal to the borax used.

Rupp and Poggendorf reported (10) that chloral hydrate reacts with both medinal and luminal in water solution, the chloral hydrate being hydrolyzed to chloroform and the barbituric acids being precipitated.

According to Ritsema (11) a precipitate occurs in the following solution on standing over night:

℞	Zinc sozoiodolic.	0.02
	Novocain	0.02
	Sol. Adrenaline (1/1000)	20.00
	Aq. borat.	15.00

The precipitate is novocain sozoiodolate. If one uses cocaine instead of novocain there is no precipitate at this concentration.

Fraase states (13) that there is no incompatibility between sodium bicarbonate and acetylsalicylic acid in capsules containing $2^1/_2$ grains of each substance, unless moisture is present far in excess of normal.

Some reports have also appeared on the stability of solutions of acetylsalicylic acid. As is well known, this substance is only slightly soluble in water, but is more soluble in solutions of sodium or potassium citrate. According to Stroud (14), in such solutions about 40% of the acetylsalicylic acid hydrolyzes into acetic and salicylic acids in three days at room temperature. If the fresh solution is boiled a few minutes, complete hydrolysis takes place, hence Stroud warns against the use of heat in preparing these solutions. Germuth (15) studied the rate of hydrolysis of acetylsalicylic acid in ethanol, glycerin, water and various mixtures of these solvents. Hydrolysis increased with time and with increasing percentage of water. A mixture of equal parts of ethanol and glycerin, in presence of water, caused slightly less hydrolysis than was brought about by either solvent alone with water. A. H. Clark (16) also worked on this problem. According to his results, the best proportions for keeping hydrolysis at a minimum are as follows: 3 parts of potassium citrate are dissolved in 15 or 20 parts of water, 1 part of acetylsalicylic acid is added, and the solution is saturated with sugar.

The precipitation of strychnine from solutions of its salts sometimes observed on addition of alkali iodides has been variously ascribed to alkalinity of the iodide, salting out of the strychnine salt, formation of the hydriodide and formation of a complex iodide. Hargreaves (17) reported that when strychnine sulphate solutions are treated with alkali iodide or HI, strychnine hydriodide is formed, having a solubility of 1 Gm. in about 345 cc. of H_2O at 25°, but much less soluble in presence of excess of soluble iodide. Strychnine periodide, of low solubility, is formed when a very dilute solution of iodine reacts on strychnine hydriodide.

Lanwermeyer reported (18) on the incompatibilities of a number of drugs including amidopyrine, acriflavine (base), acriflavine hydrochloride, anesthesin, barbital, barbital sodium, butesin, butyn, neonal, phenobarbital sodium and ephedrine salts.

Emulsions.—An interesting emulsion was described in an English article (19). The prescription was for a cod liver oil emulsion containing, among other ingredients, lime water and mucilage of acacia. The difficulty arose from the fact that emulsions made with lime water are of the water-in-oil type, while acacia emulsions are of the oil-in-water type, and two such emulsions are as immiscible as oil and water alone.

Suppositories.—Schroff (20) has contributed to our knowledge of suppositories by extending the work of Rapp, who showed that the presence of water is of greatest importance for the absorption of drugs from the intestine. Schroff indicates that suppositories with a base of cacao butter and a small amount of water may be made either as water-in-oil emulsions or oil-in-water emulsions. When quick action of a drug is desired Schroff recommends that a suppository be used in which the solution or paste of the drug is the continuous or external phase. Drugs which have a local action should be suspended or dissolved in water as the dispersed or internal phase of the suppository. Typical formulas for suppositories used by Schroff are:

Oil-in-Water Emulsion.			Water-in-Oil Emulsion.		
Natr. iod.		0.10	Natr. iod.		0.10
Aq. dest.		0.15	Aq. dest.		0.15
Lecithin		0.02	Cholesterol		0.04
Ol. cacao	*ad*	2.00	Ol. cacao	*ad*	2.00

As indicated, the nature of the emulsion depends upon whether lecithin or cholesterol is used as the emulsifying agent.

Sterilization of Solutions.—It is well known that certain solutions for injection cannot be sterilized by use of heat on account of the instability of the drug toward heat. Such solutions may be sterilized by filtration through a germ-proof filter. In an English journal, Hunwicke describes (21) the three main types of bacteria filters in use: (*a*) kieselguhr, represented by the Berkefeld filter, (*b*) porcelain (Chamberland and Doulton), (*c*) asbestos (Seitz). With the Berkefeld filter the entire apparatus must be sterilized in an autoclave. Porcelain filters are slower than the Berkefeld and the only really satisfactory cleaning process is to heat to redness in a muffle furnace. The Seitz filters are essentially discs of compressed asbestos and here again the whole apparatus must be autoclaved before use. It is stated that such solutions should not be made and dispensed by the pharmacist unless they are tested bacteriologically for sterility, because filtration is a less certain method of sterilization than heat, and contamination may occur during filling. The author states that this work requires apparatus which is hardly likely to be available in the small pharmacy, and that the difficulties cannot be overcome by makeshifts, but that the work appeals to many who are particularly interested in the professional side of their work.

There has been some demand for an autoclave that would be practical for the retail pharmacist. Greenish and Holder (22) of England have devised such an autoclave which is made similar to household pressure cookers.

For sterilization of novocain solutions, Rae suggests (23) filtration through a Chamberland filter, since heat caused decomposition, even when the solution was heated to 55–60° for one-hour periods on three successive days. However, J. Abildgaard (24) states that 2% solutions of novocain in *N*/1000 HCl suffer no appreciable decomposition when autoclaved for 20 minutes at 120° C. Eschenbrenner and Rosenberg (25) recommend that sterile solutions be prepared by combining filtration through a Seitz filter with the addition of 0.2% of Nipasol-Sodium.

Accuracy of Dispensing.—The subject of accuracy in dispensing has become a live one in the United States, following reports that of 100 prescriptions filled by 100 different drug stores in the District of Columbia, 67 were found to have been filled unsatisfactorily. The federal food and drug administration which conducted this test has jurisdiction only over drugs moving in interstate commerce and in the District of Columbia and the territories, but it was pointed out that state and city officials have authority to make similar checks elsewhere. As pointed out in the *N. A. R. D. Journal* (26) such publicity is damaging to pharmacy and every owner of a drug store should check and double check the accuracy of himself and all his clerks.

According to Butler (27) there has been considerable discussion from time to time in England as to the percentage error that should be allowed as unavoidable in the dispensing of medicines and the general opinion seems to be that an error of 10% should be allowed.

The accuracy of various methods of dividing powders was determined by J. Büchi, whose results appeared in a Swiss journal (28). Some of these methods are not used in the United States but the relative accuracy is of interest. Büchi reported that the dividing of powders with a spatula by the eye was very uncertain, the maximum error amounting to 24.5%; he recommends that this method should not be used. The use of "powder shears" is more accurate, especially in dividing crystalline powders, the maximum error being 8.7%. Another method used is to plug a cylinder with powder and divide by means of a device. In this process the error is 5.8%. Büchi states that the best method of dispensing powders is to weigh each powder. With the ordinary hand balance the error was 4.1% while with the Barnhart dispensing scales the error was not more than 1%.

Sources of Dispensing Information.—A great deal of information as to methods of filling various prescriptions appears in the questions and answers columns of pharmaceutical journals. The answers prepared by J. Leon Lascoff published in the *Practical Druggist, New York Pharmacist* and *New York Journal of Pharmacy*, and the prescriptions discussed by S. L. Hilton in the *American Druggist* are worthy of study by every prescriptionist. Owing to the large number of such prescriptions, it is beyond the scope of this report to consider them in detail here. The pharmacist may also find it advantageous to follow the new items published in the *Journal of the American Medical Association;* for example, the issues for May 1932 include such items as tincture of metaphen, and ampuls of sodium iodobismuthite and sodium iodide in ethylene glycol.

Related Investigations.—In addition to the scientific and professional studies, a great deal of information relating to various other phases of prescription work has been published during the year. Thus a number of articles have appeared dealing with methods of promoting the use of U. S. P. and N. F. items in prescriptions. C. B. Jordan published (29) a survey of the nature of the prescriptions filled and analytical work conducted in professional stores. L. A. Seltzer contributed an article (30) on prescription pricing. Monell and Brown (31) studied the average prices of prescriptions in Buffalo, N. Y., and Columbus, O. A report on the Maryland prescription count was presented (32) by R. L. Swain. E. N. Gathercoal supplied information (33) on the use of fluidextracts during the past 50 years. The preliminary report of the U. S. P.-N. F. prescription ingredient survey for 1931 appeared (34). The work of the St. Louis Drug Survey was carried on. These projects indicate that almost all phases of pharmaceutical dispensing have been actively studied during the year.

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IMPORTANT ANNOUNCEMENT!

Beginning in the July issue of the JOURNAL, the second report on the professional phase of the National Drug Store Survey of the United States Department of Commerce will be printed in several instalments. This publication, written by Frank A. Delgado and Arthur A. Kimball, is entitled: *"THE PROFESSIONAL PHARMACY."* ("An Analysis of Prescription Department Activities.")

This report is believed to be one of the most complete studies of pharmaceutical economics ever made. The information contained therein should be of practical value to all branches of the profession and industry—proprietors of professional and commercial type pharmacies, educators and students of pharmacy, wholesalers and manufacturers of pharmaceuticals. Suggestions for improved practice are made on the basis of the findings of this detailed investigation. If these suggestions are applied, it is believed that increased prescription business and volume will be realized.

Four professional pharmacies located in St. Louis, Missouri, provided the test laboratories about which the study was centered, a detailed analysis of their complete operations being made. In addition, 35 proprietors of professional pharmacies located throughout the country answered a questionnaire containing 66 questions. These questionnaire replies make it possible to present an even more complete picture of professional pharmacy operation than was at first contemplated. Wherever such information is of value, the findings in the professional pharmacies are compared with those of 13 commercial type drug stores, reported in the Survey's first publication on prescription department activities, entitled: "Prescription Department Sales Analysis in Selected Drug Stores." A large number of prescriptions, 10,000 filled by the professional pharmacies and 10,000 filled by the commercial type stores, were analyzed from every practical point of view, the results of this analysis forming one of the most important sections of the report.

Some questions which have caused much conjecture in the profession for years are authoritatively answered in "The Professional Pharmacy." For example—What are the minimum requirements to be met in opening a professional pharmacy? How can simplification of the pre-

scription department inventory be effected? What are the leading prescription ingredients—those prescribed most frequently? Does the new school of physicians, those who have graduated since the World War, lean more toward manufacturers' trade-named specialties than toward official U. S. P. and N. F. products? What changes have prescriptions undergone since 1910? What is the average cost of materials and selling price of different types of prescriptions? These and many other questions of a similar type will be answered in this publication.

After the report has been published in the JOURNAL, it will be reprinted in pamphlet form and will be available at the office of the Secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION, at a minimum price consistent with cost, to be announced later.

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5. Share of the Prescription Department in Sales Volume.
6. Number of Prescriptions Filled Daily and Annually, by Type of Prescription.
7. Prescription Business by Type of Prescription in 1910, 1920 and 1930.
8. Seasonal Demand for Prescriptions.
9. Seasonal Demand for Regular Prescriptions.
10. Seasonal Demand for Narcotic Prescriptions.
11. Seasonal Volume in Liquor Prescriptions.
12. Prescription Inventory Problems and Ingredient Analysis.
13. Opening Business and Extent of Growth of the Drug Store's Prescription Department.
14. Prescription Ingredient Requirements and Occurrence by Type of Ingredient in Professional and Commercial Type Drug Stores.
15. Frequency of Occurrence of Prescription Ingredients.
16. Number of Ingredients Required per Prescription.
17. Number of Additional Ingredients Required in Filling Successive Blocks of 500 Prescriptions.
18. Simplification of the Prescription Department Inventory.
19. Introduction of New Manufacturers' Specialties.
20. Method of Filing Information on Specialties.
21. Specification of Galenicals of Particular Manufacture.
22. Extent of Manufacturing in the Pharmacy.
23. Private Formula Prescriptions.
24. Prescription Price Trends.
    Average Price of Prescriptions by Type of Prescription in Professional and Commercial Type Drug Stores—Changing Price Trends in 1910, 1920 and 1930.
25. Monthly Prescription Price Trends in Three Additional Professional Drug Stores.
26. Price Ranges of Prescriptions by Type and Nature of Prescription.
27. Prescription Price Ranges Compared between Commercial Type and Professional Drug Stores, and for Prescriptions Filled in 1910 and 1920.
28. Inconsistency in Prescription Pricing—Prescriptions Priced below Cost.
29. Average Cost of Materials and Selling Price of Prescriptions Filled in Two Commercial Type Drug Stores, by Form and Type of Prescription.
30. Prescription Business According to the Physicians Writing the Prescriptions.
31. Extent to Which Physicians Are "Detailed" by the Pharmacist.
32. Analysis of the Prescription Business of the Leading Physicians.
33. Preference of Physicians for Official or Specialty Remedies.
34. Prescription Business by Type of Practice of the Physicians Writing the Prescriptions.
35. The Problem of Physicians' Errors in Prescription Writing.
36. Prescription Business by Form of Prescription.
37. Requirements of the Prescription Container.
38. Specialty Capsule Prescriptions.
39. Time Study of the Prescription Business in Three Professional Pharmacies.
40. Prescription Business Received by Telephone. 41. Lists of the Leading Ingredients.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1932–1933.

Office of the Secretary, 10 West Chase St., Baltimore, Md.

LETTER NO. 8.

To the Members of the Council:

57. Life Members. The following have become Life Members through the payment of dues for thirty-seven consecutive years: Josie Wanous Stuart, Minneapolis, Minn., and Benjamin Rosenzweig, Brooklyn, N. Y.; and the following through the payment of $25.00: Carl Stier, Paris, France; Arthur S. Metzger, Malden, Mo.; and Ernest G. Eberhardt, Indianapolis, Ind.

58. Northern New Jersey Branch of the A. Ph. A. Motion No. 14 (Council Letter No. 6, page 244) has been carried and the application, preamble, constitution and by-laws are approved. The meeting date of the Branch has been changed from the second to the third Monday in each month to avoid conflict with the meeting of the New York Branch.

59. North Pacific Branch of the A. Ph. A. Motion No. 15 (Council Letter No. 6, page 248) has been carried and the application, preamble, constitution and by-laws are approved.

60. Election of Members. Motion No. 16 (Council Letter No. 6, page 252) has been carried and applicants for membership numbered 66 to 99 are declared elected.

61. Distribution of Beer and Other Malt Beverages through Drug Stores. Motion No. 17 (Council Letter No. 7, page 252) has been carried, and attached are copies, for your records, of the letter sent to the presidents of the state pharmaceutical associations and of the bulletin sent to the pharmaceutical publications.

62. California College of Pharmacy Student Branch, A. Ph. A. The following application and proposed preamble, constitution and by-laws have been received:

> We, students of the School of Pharmacy of the California College of Pharmacy, desire to establish a Student Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION and hereby petition the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION to recognize us as such. The consitution and by-laws are herewith submitted for approval.
>
> August LaRosa, Jose Macias, Andrew Dunlop, William Wickwire, Raymond Leonard, Willard Larson, William Uomini, John Isi, Allen Caldeira, Eugene Bettencourt, Albert Thomas, Satoru Taoka, John Doble, Fred Yerman, Philip Blind.

PREAMBLE AND BY-LAWS OF THE UNIVERSITY OF CALIFORNIA STUDENT BRANCH OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

We, students of the College of Pharmacy (Department of Pharmacy) of the University of California, having organized a Student Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION for the purpose of identifying ourselves with those who are most active in promoting the general welfare of the pharmaceutical profession, and in so doing pledge ourselves to this end, do hereby adopt the following as our constitution and by-laws:

1. Name.—The name of this organization shall be: "The University of California, Department of Pharmacy, Student Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION."

2. Status.—This Branch shall be governed, except wherein these By-Laws differentiate, by the AMERICAN PHARMACEUTICAL ASSOCIATION. The Constitution and By-Laws of the AMERICAN PHARMACEUTICAL ASSOCIATION shall take precedence over the adopted By-Laws of this Student Branch.

3. Members.—The members of this Branch shall be elected from among the regular enrollment of students of the College who are candidates for degrees. All members must qualify and have met all the requirements for Associate Membership in the AMERICAN PHARMACEUTICAL ASSOCIATION.

4. Charter Members.—The following list of members of the Student Branch shall be forever known as Charter Members of this Branch and at no time shall this list be removed from these

By-Laws: August LaRosa, Jose Macias, Andrew Dunlop, William Wickwire, Raymond Leonard, Willard Larson, William Uomini, John Isi, Allen Caldeira, Eugene Bettencourt, Albert Thomas, Satoru Taoka, John Doble, Fred Yerman, Philip Blind.

5. Officers.—The officers of this Student Branch shall consist of a president, a vice-president, a secretary, a treasurer and an adviser or sponsor. All except the adviser shall hold office for one year; the adviser shall be retained for a period the length of which is at the pleasure of this Branch.

6. Committees.—Within five days subsequent to his election, the president shall appoint a Committee on Membership and a Committee on Program, and any other Committees deemed necessary. Each of these Committees shall consist of three members.

7. Executive Committee.—The officers of this Branch together with the chairman of the Committee on Program and the Committee on Membership shall constitute an Executive Committee. All necessary business shall be transacted by the Executive Committee.

8. Meetings.—The meetings of this Branch shall be held the first Wednesday of each month of the regular academic year. Special meetings may be called by the president at such times and places as the Executive Committee may deem desirable and must be called upon the written request of seven members of the Student Branch. A special meeting for the purpose of installing officers for the coming year shall be held within two weeks after the regular election of officers; date of said special meeting shall rest with the president who shall act upon the advice of the Executive Committee.

9. Elections.—Elections of officers, with the exception of the Adviser or Sponsor, shall be by ballot. Voting by proxy shall not be allowed and said election shall be held at the last regular meeting of the academic year. Vacancies shall be filled by the Executive Committee in all cases with the exception of the president. The vice-president shall succeed the president in the event of his inability or absence. The Executive Committee may rule on the ability of the president or other officers; neglect of duty by any officer may result in his recall by a $^2/_3$ (two-thirds) vote of the Executive Committee. The selection of an adviser or sponsor, who shall of necessity be a member of the faculty of the College or a Graduate Student in good standing, shall rest in the hands of the Executive Committee.

10. Quorum.—Fifty per cent of the members shall constitute a quorum.

11. Order of Business.—(*a*) Call to order; (*b*) Reading of the minutes of the previous regular meeting; (*c*) Unfinished business; (*d*) New business; (*e*) Program; (*f*) Nomination and election; (*g*) Adjournment.

12. Amendment.—These by-laws shall be adopted, revised or amended only upon a $^2/_3$ (two-thirds) vote of the total qualified membership of this Student Branch. No amendment shall be considered that in any way violates any written or implied regulation of the By-Laws and Constitution of the AMERICAN PHARMACEUTICAL ASSOCIATION.

(*Motion No. 18*) *It is moved by Kelly that the application for the formation of the California College of Pharmacy Student Branch, A. Ph. A., and the proposed preamble, constitution and by-laws be approved.* A vote on this motion is called for at this time but will be considered as tentative if there is objection or if any member wishes to discuss it.

63. Annual Joint Meeting Executive Committee N. A. R. D. and Council A. Ph. A. This annual joint meeting will be held this year at the A. PH. A. meeting and arrangements have been completed to hold the joint session on Wednesday afternoon, August 30th, at 3:00 o'clock. It is included in the general program.

64. Applicants for Membership. The following applications properly endorsed and accompanied by the first year's dues have been received:

No. 100, Benjamin Agrant, 410 West 12th St., Sioux Falls, S. D.; No. 101, Frederick J. Ahlfs, P. O. Box 87, Conde, S. Dak.; No. 102, Martin G. Albaugh, 458 W. Ninth St., Erie, Pa.; No. 103, Otto Bark, 11724 Normal Ave., Chicago, Ill.; No. 104, C. A. Benson, Maitland, Fla.; No. 105, Eugene D. Bettencourt, P. O. Box 140, Centerville, Calif.; No. 106, George Philip Blind, 55 Crane St., San Francisco, Calif.; No. 107, Kelly Boy, 1714 Monroe St., Pullman, Wash.; No. 108, Charles Buck, 725 6th St., Brookings, S. Dak.; No. 109, Henry H. Busby, P. O. Box 211, Evanston, Ill.; No. 110, Allen Caldeira, P. O. Box 119, Centerville, Calif.; No. 111, F. L. Christenson, Idanha Pharmacy, Lewiston, Idaho; No. 112, C. F. Clancey, Jr., 1306 E. 9th St., Sioux Falls, S. Dak.; No. 113, George F. Clayton, 1737 Van Buren St., Bronx, N. Y.; No. 114, J.

R. DeSaxe, Paris Medicine Co., St. Louis, Mo.; No. 115, John Doble, 1441 Clay St., San Francisco, Calif.; No. 116, Andrew M. Dunlop, 860 Ashbury St., San Francisco, Calif.; No. 117, Lawrence Francis Ferring, Washington & Pine Sts., New Orleans, La.; No. 118, Paschal L. Guerriere, 4134 Sheridan Blvd., Denver, Colo.; No. 119, Abraham Kaliel Haggar, 1201 East 8th St., Sioux Falls, S. D.; No. 120, Thomas K. Haggar, 1201 East 8th St., Sioux Falls, S. D.; No. 121, Albert C. Hawes, 100 West 46th St., Bayonne, N. J.; No. 122, Emil A. Hayden, 652–654 Williamson St., Madison, Wis.; No. 123, Allen Loy Hess, 54–56 Spring St., Eureka Springs, Ark.; No. 124, Manuel Garcia Hernandez, Obispo 16, altos, Habana, Cuba; No. 125, John J. Isi, 58 Dolores Terrace, San Francisco, Calif.; No. 126, Ernest Jacob, Jr., Washington & Pine Sts., New Orleans, La.; No. 127, Harold A. Johnson, 911 W. Johnson St., Madison, Wis.; No. 128, George R. Jones, Archer, Fla.; No. 129, Learny F. Jones, 800 E. Market St., Indianapolis, Ind., No. 130, Arthur Richard Karuzas, 125 E. Main St., Amsterdam, N. Y.; No. 131, Leo H. Kramer; 270 Lombard St., Pittsburgh, Pa.; No. 132, Carl H. Krueger, Minocqua, Wis.; No. 133, Eugene C. Kuske, 303 E. Walnut St., Sleepy Eye, Minn.; No. 134, August LaRosa, 364 Precita Ave., San Francisco, Calif.; No. 135, Willard F. Larson, Route 2, Box 54, Redwood City, Calif.; No. 136, Raymond Leonard, 54 Woodland Ave., San Francisco, Calif.; No. 137, Alfred A. Lippe, 22–38—31st Street, Astoria, N. Y.; No. 138, James W. McCormley, 618 Short St., Wilson, Pa.; No. 139, Thomas W. MacWilliam, 1257—3rd Ave., San Francisco, Calif.; No. 140, Jose Macias-Sarria, 1902 Page St., Apt. 8, San Francisco, Cal.; No. 141, Heinrich Martens, 1117 N. 8th St., Sheboygan, Wis.; No. 142, George Mittermann, Jr., 815 Rebecca Place, Elizabeth, N. J.; No. 143, H. Neamtan, 64 Prince St., Montreal, Canada; No. 144, Alvin E. Olson, 901—6th St., Brookings, S. Dak.; No. 145, Frank J. Pokorny, 115 W. 68th Street, New York, N. Y.; No. 146, Henry Edward Rakeman, Jr., Ennis, Mont.; No. 147, Claude M. Reed, Main Street, Jefferson, N. Y.; No. 148, Stephen W. Sabo, 1915 W. 54th St., Cleveland, Ohio; No. 149, Joel J. Schwarz, 18 Renner Ave., Newark, N. J.; No. 150, George Louis Secord, 2324 Lawrence Ave., Chicago, Ill.; No. 151, Robert A. Stauber, 115 W. 68th St., New York, N. Y.; No. 152, Maurice R. Smith, 728 Medary Ave., Brookings, S. Dak.; No. 153, J. Stanley Steiner, 225 Church St., South Amboy, N. J.; No. 154, Oscar Paul Stults, Vernon, Colo.; No. 155, Satoru Taoka, 1740 Post Street, San Francisco, Calif.; No. 156, Albert R. Thomas, 346 Franklin St., Napa, Calif.; No. 157, Wm. Uomini, 121 Los Banos Ave., Daly City, Calif.; No. 158, Wm. D. Wickwire, 400 Kirkham St., San Francisco, Calif.; No. 159, Fred Yerman, 576—55th Street, Oakland, Calif.; No. 160, Felix A. Zuchowski, 1214 Cascade St., New Castle, Pa.

(*Motion No. 19*) *Vote on applications for membership in the American Pharmaceutical Association.*

E. F. KELLY, *Secretary.*

NEW YORK PHARMACEUTICAL CONFERENCE.

More than 2500 independent retail pharmacists representing pharmaceutical associations in New York, New Jersey, Pennsylvania, Massachusetts, Connecticut and Maine, in a mass meeting at the Hotel Pennsylvania on Tuesday night, June 6th, adopted a tentative code of fair competition for the pharmaceutical industry in line with the proposed National Industry Control Bill. The meeting was held under the auspices of the New York Pharmaceutical Conference, official trade and professional organization of the independent retail pharmacists of New York City and Westchester County.

Former Congressman F. H. La Guardia, addressing the delegates, declared that the health of the people of this country required the enactment of legislation prohibiting the sale of medicinal items in any but registered pharmaceutical outlets. He warned his hearers that the pharmaceutical profession would inevitably deteriorate unless such legislation was placed on the statute books of the various states.

"One of the most serious conditions confronting the pharmaceutical industry of this country is the over-production of outlets where pharmaceutical items are distributed," he said. "I am in favor of legislation that would limit the number of licensed pharmacies according to population. Let department stores sell their socks and bloomers, cosmetic shops their perfumes and face powders but when it comes to the sale of medicines, drugs and pharmaceutical preparations, these should be dispensed by men trained for the task in the pharmaceutical colleges of our country."

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meeting of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter.

BALTIMORE.

The May meeting of the Baltimore Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held May 12th, at the Emerson Hotel. President Solomon was in the chair.

The speakers of the evening were Dr. S. L. Hilton of Washington, D. C., and Mr. Marvin J. Andrews of the School of Pharmacy, University of Maryland.

Doctor Hilton spoke on scientific pharmacy and prescriptions. From many years experience in the retail business he cited several interesting and unusual prescriptions and explained how they should be properly filled. Attention was called to the unsatisfactory conditions prevailing in the compounding of chemicals which change in weight as a result of climatic conditions. In his work on the Committee on Prescription Tolerances of the A. PH. A. Doctor Hilton made note of the progress being made to correct inaccuracies in compounding.

Mr. Andrews presented a lengthy paper describing the fine work which is being carried out under his direction at the School of Pharmacy. Work on the magnitude of error of dispensing of powder prescriptions was reported. The influence of methods of filling, number of ingredients of each prescription, nature of the ingredients, number of powders made and the amount of material in each powder, as factors in the production of error was brought out. As the result of careful examination of 450 powder prescriptions filled by the senior students in dispensing pharmacy at the School, it was concluded that twice the average standard deviation would be a reasonable error.

The work being carried out in this field is particularly valuable. All the years that prescriptions have been filled and still no one knows just how accurate a properly compounded prescription should be. It is to be hoped that the work of the Committee of Prescription Tolerances will lead to a satisfactory conclusion.

Following the presentation of papers discussion was entered into by those present. It was the consentient opinion of those present that more prescription survey work should be carried out in order that our Law Enforcement Officials might have a standard to apply in their work.

The meeting was attended by about seventy-five members and their friends including students from the School of Pharmacy and the School of Medicine, University of Maryland. A vote of thanks was tendered the speakers.

C. JELLEFF CARR, *Secretary-Treasurer.*

CHICAGO.

The 214th meeting of the Chicago Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at the University of Illinois College of Pharmacy on the evening of May 16th.

President Terry introduced the speaker of the evening, Dr. Bernard Fantus.

Dr. Fantus spoke on the subject, "Medicinal Vehicles, an Experimental Study." He discussed first the U. S. P. Aromatic Elixir.

Five formulas for the making of the elixir were discussed, each aiming at shortening the time of manufacture. All of the ways suggested were uniform in the one respect, that the syrup or sucrose was added last so as to reduce the viscosity of the liquid so that it would filter faster. Dr. Fantus offered his own formula which does not require the use of talc as a filtering medium. He claims that the talc removes not only the undissolved oils but some of the dissolved oils.

Iso-Alcoholic Elixir was next discussed. This is composed of two elixirs, one of high alcoholic strength and one of low alcoholic strength, the two to be mixed in the proper ratio to conform to the alcoholic strength of the liquid medicament for which the elixir is to be used as the vehicle. Samples of potent fluidextracts mixed with U. S. P. Aromatic Elixir and mixed with the Iso-Alcoholic Elixir were passed around to the audience and the results were quite evident.

The advantage of this proposed elixir was shown with the use of Sodium Bromide, Chloral Hydrate and Phenobarbital.

An Aromatic Syrup of Yerba Santa was discussed and its power of disguising bitter drugs was shown. Wooden spoons were passed around to the audience so that the samples could be tasted.

Syrup of Glycyrrhiza was the next vehicle discussed. It was found that some samples of the Fluidextract and Fluidglycerate were sweet while some were bitter and tests showed this to be in the rhizome of the drug. Since no uniform sweetness could be expected from the drug, Dr. Fantus extracted the sweet principle of the drug, glycyrrhizin, and made a syrup from it. This new syrup has the advantage in that it is always sweet and, in later discussions, was shown to be even cheaper to manufacture than the official syrup.

Syrup of Anise was next presented as a vehicle to replace Elixir of Anise.

The last vehicle discussed was Syrup of Cinnamon. This new syrup is made with the oil and Compound Tincture of Cudbear, the oil replacing the drug. This is a more rapid way of making the syrup and has the advantage in that it is more pleasant to take, not astringent, and offers no incompatibility with iron preparations.

The discussion following the demonstration brought out many interesting bits of information. Considerable interest was manifest in the suggested use of amaranth as a coloring agent replacing cudbear.

Dr. Fantus expressed his appreciation of the aid received from his assistants, the Misses Dyniewicz.

LAWRENCE TEMPLETON, *Secretary.*

NEW YORK.

The May meeting of the New York Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held on May 8th, at the New York College of Pharmacy, Columbia University. About eighty-five members and guests were present. The president, Dr. Ernst Bilhuber, presided. The report of the secretary was read and approved.

Chairman Mayer, of the Audit Committee, reported approval of all bills submitted, and Treasurer Currens reported a balance of $273.49.

Chairman Lehman, of the Committee on Education and Legislation, reported:

State Legislation.—Out of the 85 odd bills affecting Pharmacy, presented in the last State Legislature, only one has passed and is now a law, namely, the Narcotic Bill; the only difference between the new law and the Harrison, is that it includes Cannabis Indica and its derivatives, and does exempt such preparations which contain more than one narcotic, when they contain only exempt quantities of each narcotic ingredient. The inclusion of Cannabis does not bother the New York City pharmacist, as it is already included in the Sanitary code of the Health Department of this City.

Sales Tax.—This law affects pharmacists as well as other retail merchants; foods are exempted from its provisions, and an earnest effort is being made by the New York State Pharmaceutical Association as well as the N. Y. Pharmaceutical Conference to exempt at least prescriptions from its provisions.

Medicinal Liquor Regulations.—No longer will a duplicate form 1403 be given to the patient; physicians may use the duplicate official form as an original, by crossing out the word Duplicate. After January 1, 1934 physicians need not use official blanks, but will be provided with a stamp which must be affixed to their own prescription blanks. Physicians may prescribe sufficient medicinal liquor or wine of over 3.2 to last the patient for 30 days, estimated about two gallons per month. Physicians may prescribe sufficient for 90 days, but in such cases must immediately

notify the Supervisor of Permits for the district of his action, and the pharmacist filling such prescription must do so likewise. Prescriptions for medicinal liquors are valid for seven days after their date. Physicians need not make reports, but pharmacists must; physicians must keep an alphabetical record of all their prescriptions of that kind.

Dealers in Malt Liquors.—Such must pay an annual excise tax of $20.00, except when they have a so-called retail liquor dealer's license, then there is no additional fee.

(The New York State Law names the Pharmacists and Grocery-men as the distributors of Malt Liquors and Wines under 3.2 strength when the beverages are not to be consumed on the premises. License fee, $50.00 a year in places of more than 1500 inhabitants; less, $25.00.)

Chairman Kidder, of the Professional Relations Committee, reported that a joint Physician-Pharmacist meeting was being organized by the New York Conference, Academy of Pharmacy, and the State Association. He suggested that the Branch coöperate with these other organizations in one big meeting. Dr. Kidder was authorized to go ahead with his plans.

Chairman Kassner submitted the application of Prof. Leonard J. Piccoli for membership in the Branch; he was elected.

Dr. Schaefer next reported that the Northern New Jersey Branch changed its proposed meeting night to the third Monday of each month. It was proposed, and approved, to send a delegation from the New York Branch to attend the first meeting of the Northern New Jersey Branch.

Dr. Schaefer reported for the Remington Medal Committee that the medal had been awarded to Secretary E. F. Kelly, of the AMERICAN PHARMACEUTICAL ASSOCIATION. After a discussion, President Bilhuber, appointed Dr. Schaefer to take care of arrangements for a suitable meeting to be held early in the fall at which time the medal would be given to Dr. Kelly. The members were of the opinion that this meeting should be held in New York.

Chairman Heimersheim of the Committee on the Progress of Pharmacy submitted a report summarized as follows:

An investigation of the keeping qualities of Syrup of Ferrous Iodide discloses the fact that oxidation of the iron is less rapid in syrups containing citric acid than in syrups containing phosphorous acid.

Ballard and Miller, in an article in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, call attention to the fact that Tolu concentrates from several reputable manufacturers, when diluted according to directions, yield syrups containing considerably less alcohol than required by the U. S. P. for Syrup of Tolu.

Dr. Bilhuber then introduced the speaker for the evening, Harry Taub; his subject was "Chemical Microscopy in the Service of Pharmacy." He pointed out how chemical microscopy got its start by the following incident. A museum had purchased an alleged ancient Roman coin; subsequent information had made the director suspicious of the genuineness of his specimen. A chemical analysis of its composition would provide the necessary information and the coin was taken to Professor Chamot of Cornell for chemical analysis. Now this would ordinarily be a simple procedure, but Professor Chamot was told that the coin must under no circumstances be mutilated. He finally solved the problem by examining microscopically the metallic mark left on a ground glass plate, when the plate was scratched with the coin. The entire chemical analysis was carried out under the microscope.

Since then an entire scheme of inorganic analysis has been devised for application to the microscope. The speaker called particular attention to the fact that the identification of many compounds is facilitated through the use of the microscope, in that the crystal forms of the various materials can be used in conjunction with other properties as a reliable unique characteristic. The processes of distillation, filtration, sublimation and others can be carried out on minute quantities of materials. The speaker demonstrated the processes. The microscope makes possible the use of polarized light in the identification of many substances. Another point which Professor Taub emphasized was that rarely are complete separations necessary in the identification of substances in a mixture. The tests applied are easily interpreted without making unnecessary long and tedious separations.

Throughout the course of his talk the speaker demonstrated the operations—the detection of traces of "Bichloride" in Calomel was shown by sublimation from the suspected sample on to the surface of a glass slide. Tests of identity are then run on the minute amount of sublimate so obtained.

Another interesting application discussed was a case of belladonna poisoning from a sample of Elixir I.Q. and S. Micro tests carried out on the sample finally proved the presence of both atropine and aconitine. The usual routine chemical analysis would have been extremely long and tedious, with the likelihood that the infinitesimal amount of aconitine which was present would be overlooked. The micro method readily and conclusively proved the presence of both of the alkoloids.

Another advantage of micro-chemical analysis is the simplicity of the equipment necessary. Aside from the microscope, the necessary materials are, about sixty reagents, glass slides, cover-slips, capillary tubes, small glass rods, a small spirit lamp or micro-burner and a set of substances for comparison tests.

Micro-chemical analysis has proved to be especially useful in distinguishing counterfeit proprietaries from the genuine. When the product is a tablet, the diluent is frequently used as an index of genuineness, or the degree of fineness of the particles serves as an index. Examination of the type or ink used in decorating the package has been used as a means of distinguishing genuine from counterfeit. Liquid preparations often contain a secret identifying substance; face powders can readily be differentiated under the microscope and qualitative examination has been facilitated through the use of microchemical methods.

An extremely interesting application of micro-chemistry, demonstrated by Professor Taub, was the detection of blood stains with the crystal-hæmin test. Every variety of blood gives a different reaction. It is possible to differentiate the blood of males and females by this test. The character of the crystal formed is the distinguishing point.

By means of a special projector, the speaker assisted by Mr. Rosenberg was able to show pictures of various crystals.

The applications of micro-photography were briefly touched upon, and Professor Taub cited some interesting cases where micro-photographs proved very useful in legal work. Micro-chemistry has also proved its worth in fields other than pharmacy. The speaker referred to the use of the microscope in the fur industry as a means of identifying various furs before and after dyeing; in the textile trades—in the examination of fibres—rayons, silks, wools and cottons are easily distinguished, and mixtures of these fibres can be detected.

Professor Taub called attention to the importance of a knowledge of crystallography in micro-chemistry, and since the crystal-form becomes a distinguishing character a knowledge of the classification of crystals is essential.

The numerous demonstrations throughout the talk were obviously followed with interest and the display of equipment was enthusiastically examined by many.

Following a brief discussion a rising vote of thanks was accorded the speaker.

RUDOLF HAUCK, *Secretary.*

NORTH PACIFIC.

The second meeting of the North Pacific Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at North Pacific College of Oregon, April 24, 1933, President A. O. Mickelsen presiding.

Secretary Donnell read a letter received from Secretary E. F. Kelly announcing that the application of the North Pacific Branch and its constitution and by-laws had been approved by the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION and the Branch was officially established. Letters of congratulation and good wishes for the success of the North Pacific Branch were read from W. Bruce Philip and Prof. C. Leonard O'Connell.

The president appointed the following committees:

Committee on Practical Pharmacy: *Chairman,* Harry Weis, 639 Webster St., Portland; Frederick Grill, Portland; Walter Rhodes, Portland.

Committee on Professional Relations: *Chairman,* L. G. Haack, 423 Taylor St., Portland.

Committee on Program: *Chairman,* Earl Gunther, 404 Taylor St., Portland; Fred Felter, 503 Woodlark Bldg., Portland; F. A. Geue, 448 Stark St., Portland.

Committee on Membership: *Chairman,* Frank Nau, 127 Sixth St., Portland; Adolph Ziefle, Corvallis, Ore.; A. O. Mickelsen, Portland.

Considerable discussion was devoted to a tentative program for the Oregon State Pharmaceutical Association. North Pacific Branch will be allowed one-half day of the convention time. The program committee

pledged a program of special interest to the drug trade and professional in scope. A prescription pricing contest will undoubtedly be part of the program. Another feature proposed is a talk on "Druggists Own Products"—useful formulas coupled with a display of preparations, conducted by Dean Mickelsen.

The serving of beer by the glass over the counter was denounced by all members present. John Witty moved, seconded by Walter Rhodes, that the North Pacific Branch endorse the stand taken by the AMERICAN PHARMACEUTICAL ASSOCIATION concerning the sale of beer in the drug store.

Bulletins on the Control and Extermination of Clothes Moths were distributed by A. O. Mickelsen, bringing out the fact that now is the time to obtain new professional business by selling products made by the pharmacists for this purpose. A number of practical moth exterminators were displayed, which had been prepared by the senior pharmacy students at North Pacific College of Pharmacy.

HARVEY J. DONNELL, *Secretary-Treasurer.*

A CENTURY OF PROGRESS INTERNATIONAL EXPOSITION.

Beams from the star Arcturus set in motion the Century of Progress; newspaper and radio accounts gave a most interesting story of the event. The chairman of the Committee on Pharmacy Exhibit is H. C. Christensen and the secretary is Dr. Frank B. Kirby; this exhibit is now complete and with various displays constitutes an interesting part of the Exposition. A model of the Pharmacy Building is part of the exhibit—see May issue of the JOURNAL. History and progress of pharmacy is shown in several divisions—historical, educational and professional and includes the story of the United States Pharmacopœia and the National Formulary; there is a reproduction of part of the Ebers Papyrus. An historical drug store, and a reproduction of Chicago's first drug store, a small log building opened in 1832 by Philo Carpenter in Lake Street between what is now Wells and La Salle Streets. This is contrasted with an up-to-date pharmaceutical laboratory with modern equipment. Daily demonstrations are given in this laboratory by pharmacists on prescription compounding, testing drugs and preparations for purity, chemical problems, accuracy in weighing, etc. All of this work is of such a type as to be readily understood by the public.

The educational display shows, by means of an arch, the basic sciences on which the practice of pharmacy rests. Two 18-inch revolving globes with a map of North America contrast the number of colleges of pharmacy a century ago with those of to-day. The center of attraction for this exhibit is the model of the Pharmacy Headquarters' Building.

The exhibit also tells the story of Digitalis, from field to finished product. This is in the form of a dioramic view showing a field of digitalis, with a pharmaceutical manufacturing establishment in the background with an open front to show various divisions—drying cupboards, cleaning room, milling room, etc., and then a display of specimens of the drug in various forms from the crude state to the finished product.

An S. V. E. automatic pictural projector is used to tell the story of the U. S. P. and N. F., legislation protecting the public and safeguarding the sale of poisons and drugs, service rendered to the public and other themes.

PHARMACOPŒIAL STANDARDS.

In the discussion at the Scientific meeting of the American Drug Manufacturers' Association, Dr. Joseph Rosin brought out a point which can be quite far-reaching in its effect. He said that "the U. S. Pharmacopœia contains in its monographs statements that are not part of the standard, but embody useful or incidental information regarding the product in question. Thus, that digitalis should be stored in air-tight containers and kept free from moisture might merely mean that the product should be kept free from moisture, and that the air-tight containers are an aid in keeping it so. In dry places, the air-tight containers would not be necessary. This type of information will be appreciated by those enforcing drug standards, and probably the only way in which this could be done is to have this information so marked in the forthcoming revision of the Pharmacopœia."

EDITORIAL NOTES

Editor: E. G. Eberle, 10 West Chase Street, Baltimore, Md.

Members of the Council, A. PH. A.: S. L. HILTON, *Chairman;* CHARLES H. LAWALL, *Vice-Chairman;* E. F. KELLY, *Secretary;* H. V. ARNY, A. G. DUMEZ, H. A. B. DUNNING, WILLIAM B. DAY, C. E. CASPARI, J. H. BEAL, T. J. BRADLEY, AMBROSE HUNSBERGER. *Ex-Officio Members:* W. BRUCE PHILIP, *President;* ROWLAND JONES, G. H. GROMMET, *Vice-Presidents;* C. W. HOLTON, *Treasurer;* E. G. EBERLE, *Editor of the Journal;* A. G. DUMEZ, *Editor of the Year Book;* J. W. SLOCUM, *Chairman of the House of Delegates.*

Collaborators: The Members of the Council; E. FULLERTON COOK, *Chairman,* U. S. P. Revision Committee; E. N. GATHERCOAL, *Chairman,* N. F. Revision Committee; Chairmen of the Sections, A. PH. A.: W. J. HUSA, W. J. RIVARD, W. PAUL BRIGGS, LEON MONELL, LOUIS GERSHENFELD, CHARLES H. STOCKING, *President,* A. A. C. P.; CHARLES B. JORDAN, *Chairman,* Executive Committee, A. A. C. P.; CLARE F. ALLAN, *President,* N. A. B. P.; HENRY C. CHRISTENSEN, *Secretary,* N. A. B. P. Scientific Section—Board of Review on Papers: *Chairman,* L. W. ROWE, Detroit, Mich.; JOHN C. KRANTZ, JR., Baltimore, Md.; F. J. BACON, Cleveland, Ohio.

MEMBERSHIP PRIZES IN THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The JOURNAL will be pleased to have advice relative to membership prizes in the AMERICAN PHARMACEUTICAL ASSOCIATION, publication will be made in a succeeding issue of the JOURNAL. The following announcements have been received:

Duquesne University, School of Pharmacy, has awarded membership prizes in the AMERICAN PHARMACEUTICAL ASSOCIATION to Martin G. Albaugh of Erie, Pa., for excellence in the Department of Materia Medica, award being made by Prof. H. W. Werner. For excellence in Pharmacy, awarded by Prof. W. A. Jarrett to James W. McCormley, Wilson, Pa. For excellence in Chemistry, awarded by Dean Hugh C. Muldoon, to Felix A. Zuchowski of New Castle, Pa.

Membership prizes have been awarded at the College of Pharmacy of the State University of Iowa, as follows:

By Dean Teeters for recognition and description of organic drugs to Irvin V. Wolf. By Prof. Zada M. Cooper to John X. Power for highest rank in second-year Operative and Manufacturing Pharmacy.

A year's subscription to the JOURNAL OF THE A. PH. A. was given by Professor Kuever to Benjamin S. Goldstein, Rochester, N. Y., for first-year Operative Pharmacy. The latter also earned the prize of $20.00 given by Delta Chapter of Rho Chi in recognition of the highest average in all first-year subjects.

Massachusetts College of Pharmacy has awarded prizes consisting of nominations to membership and a year's dues in the AMERICAN PHARMACEUTICAL ASSOCIATION. These prizes are awarded to members of the graduating class who have made good averages on the senior work in all subjects and exceptional records in separate subjects, as noted:

Pharmacy, offered by Professor La Pierre, and awarded to Frank R. Crotty. Organic Chemistry, offered by Treasurer Gammon, and awarded to Edwin A. O'Hara. Materia Medica, offered by President Glover, and awarded to Samuel Mushlin. Commercial Pharmacy, offered by Vice-President Ellis, and awarded to Barnet Shapiro. Analytical Chemistry, offered by Dean Bradley, and awarded to Joseph A. Conway.

CONGRESS OF MILITARY MEDICINE AND PHARMACY.

The Seventh International Congress of Military Medicine and Pharmacy, under the presidency of Dr. José Gonsalez-Granda, Inspector of Military Hygiene, was held at Madrid, May 29th to June 4th. The outstanding entertainment function was held in the National Palace when the members of the Congress were received by the President of the Republic, S. E. D. Niceto Alcala-Zamora; thirty-five nations were represented.

During the sessions of the Congress, Government officials, including the President participated. The program included the reading of official reports, the holding of scientific discussions and attendance at demonstrations given at a large number of national and public institutions, municipal and private laboratories, sanatoriums, clinics and manufactories. The subjects referred to the Congress from

The Hague for particular discussion included "The Value of Preventive Inoculations," "The Organization of Surgical Measures of Urgency in Outposts," "The Preparation and Conservation of Rations" and "Odontological Service." No official representatives of American pharmacy attended, however the United States had representatives from the Medical Service. The president of the British Pharmaceutical Society, F. Gladstone Hines, an honorary member of the AMERICAN PHARMACEUTICAL ASSOCIATION, attended the sessions; he was made an honorary life member and presented with a medal.

The pharmacy section held its sessions at the Faculty of Pharmacy and the Municipal Chemical Laboratory; visits were made to the Central Laboratory of Medicaments, where medical and pharmaceutical supplies are prepared for the Spanish Military Service.

PHYSICIANS AND PHARMACISTS ARRANGE MEDICINE COSTS.

Doctors and druggists of Kitchener and Waterloo (Canada) have reached an agreement on prices of medicines for patients under direct medical relief and the plan, according to the *Canadian Pharmaceutical Journal*, seems satisfactory. A schedule of charges has been adopted under which the druggist bills the doctor and the latter includes this amount in his own bill. It is provided that standard pharmaceuticals be prescribed and the prescriptions limited to the needs of the case so as to prevent wastage as far as this is possible.

PERSONAL AND NEWS ITEMS.

PROFESSOR H. G. GREENISH RETIRES.

Prof. H. G. Greenish, after 43 years of service on the staff of the School of Pharmacy (British Pharmaceutical Society) and as dean for many years, has retired. We quote the following from resolutions adopted by the Society:

"As its Dean, he has been to a large extent instrumental in making the School a vital influence for propagating through British pharmacy a loyalty to the Society and to its ideals. By reason of his kindly personality and the length of his pharmaceutical career, he has ensured for himself a place in the memory of pharmacists the world over. He will be remembered for his scientific attainments, for his leadership in pharmaceutical education and above all for his personality."

Dr. J. H. Burn, M.A., M.D., has been appointed successor of Dean Greenish. The latter has been an honorary member of the AMERICAN PHARMACEUTICAL ASSOCIATION for two decades.

Robert L. Swain, *president-elect* of the AMERICAN PHARMACEUTICAL ASSOCIATION, has been appointed to the Chair of Pharmaceutical Law at Temple School of Pharmacy; he holds the degree of Bachelor of Laws from the University of Maryland. Other activities and appointments have been heretofore referred to, a number of these speak for his eminent qualification for the appointment. He is Deputy Food and Drug Commissioner of Maryland and was instrumental in establishing the Conference of Pharmaceutical Law Enforcement Officials.

Dean Henry S. Johnson of the Connecticut College of Pharmacy received the degree of Doctor of Philosophy at the Yale Commencement on June 21st. The title of his dissertation was "Some New Derivatives of Morpholine." He received his Bachelors degree at Yale in 1919 and his Master of Science degree there in 1922. Dr. Johnson held the professorship of Organic Chemistry at the University of Puerto Rico and was head of the Chemistry department at the New Haven High School prior to his connection with the Connecticut College of Pharmacy.

Dr. Robert P. Fischelis, secretary and chief chemist of the Board of Pharmacy of the State of New Jersey, delivered the commencement address to the graduating class of the Connecticut College of Pharmacy at New Haven, on the evening of June 5th. His subject was "Pharmacy's Contribution to Public Health Service."

The *Year Book* of the Medical College of Virginia for 1933, the "X-Ray," is dedicated to **Prof. W. G. Crockett.** He is a member of the Revision Committee of the U. S. Pharmacopœia and his activities in Section work of the A. PH. A. are well and favorably known.

Temple University conferred the Honorary Degree of Doctor of Science, at its Commencement Exercises, June 15th, on Dr. E. F. Kelly, Secretary of the A. PH. A. Honorary degrees were also awarded to Dr. Charles R. Mann, director of the National Council on Education; Thomas S. Gates, president of the University of Pennsylvania; William Rowen, president of the Philadelphia Board of Education; and Edward Ellsworth Hipsher, authority on Music Education.

The degree of Master of Pharmacy was conferred June 7th by the Philadelphia College of Pharmacy and Science on **Dean Theodore J. Bradley,** Massachusetts College of Pharmacy; **Henry K. Mulford,** director of the biological and research laboratories of the National Drug Company, and **Jacob L. Nebinger,** for many years a retail pharmacist in Philadelphia.

Dean Robert C. Wilson was elected *First Honorary Member* of the University of Georgia School of Pharmacy.

Dr. Lyman J. Briggs has been nominated by President Roosevelt to be Director of the Bureau of Standards, a post which he has filled as acting director since the death of Dr. George K. Burgess in July 1932. He has been in the government's scientific service for more than thirty-five years, and for several years past has been assistant director of the Bureau of Standards.

B. E. Holzendorf is pharmacist, U. S. Quarantine Station, Staten Island, to whom credit is due for work in perfecting the rat proofing of ships. A description of the method is published in *Public Health Reports* No. 20, May 19, 1933; a model is part of the exhibit of the U. S. Public Health Service in the Government Building, Chicago.

Thomas H. Allen, pharmacist, Oswego, Ore., saved the life of a young man whose jugular vein was severed in an automobile accident. Knowledge of "first aid" enabled Mr. Allen to stop the flow of blood until a physician arrived; the former has been recommended for a "Carnegie Hero Medal."

D. D. Turner, on the staff of the College of Pharmacy, University of Minnesota, for more than 20 years, has retired. The faculty and College tendered him a testimonial luncheon June 8th; Dean Wulling presided as toastmaster and members of the faculty paid tribute to the honored guest.

Robert L. Swain, Jr., son of the *president-elect,* A. PH. A., was a member of this year's West Nottingham Academy graduating class. The Academy was founded in 1741 and its history is of interest to pharmacists because Dr. John Morgan was a student there; two signers of the Declaration of Independence are among its alumni—Benjamin Rush and Richard Stockton. A number of friends attended the closing exercises; the Lieutenant Governor of Pennsylvania was the principal speaker.

R. D. Keim has been elected vice-president of E. R. Squibb & Sons.

We are indebted to Dr. Hans Meyer, editor of the *Apotheker-Zeitung,* for a mimeographed copy of the constitution, organization, aims and purposes of the "Standesgemeinschaft Deutscher Apotheker."

Dr. C. Rufus Rorem has favored us with a copy of "The Economic Aspects of Medical Services."

Dr. David Fairchild, veteran plant explorer of the U. S. Department of Agriculture, is to receive the Public Welfare Medal of the National Academy of Sciences. The medal is given for eminence in the application of science to the public welfare.

The *Long Beach Sun* (Calif.) of recent date has an editorial on "The Indispensable Druggist" in which the services of the pharmacist are depicted. The editorial follows the lines heretofore quoted—"On the development of drugs and their uses depend to a considerable extent the health and the welfare of the people of the world."

WALTER D. ADAMS.

The former president of the A. PH. A. is shown above in the regalia of Houston pharmacists for ceremonial occasions; they bestowed the insignia at the recent State convention of Texas Pharmaceutical Association.

The Wisconsin Druggist, Volume 1, No. 1, of April 1933, has been received. The Editor is **Ralph W. Clark** of the State University. The Editor and the Association have an opportunity in the great work of promoting professional pharmacy for which good wishes are extended.

Leon M. Monell, University of Buffalo School of Pharmacy, reported, at the annual convention of the New York State Pharmaceutical Association, the findings of a one-year survey of retail pharmaceutical conditions in New York State. The survey was conducted by the Committee on Pharmaceutical Economies of the New York Pharmaceutical Association.

Merck & Company's Exhibit includes a pharmacy desk with a professional pharmacist constantly in attendance, attracting considerable attention. In the presence of the onlookers the pharmacist demonstrates the art of his profession in the preparation of pills, the weighing of very small quantities of powders, the filling of capsules and the preparation of other types of pharmaceutical products required in prescriptions. A Nososcope (stereopticon) enables visitors to view the history and progress of diseases.

Burroughs Wellcome & Co. show outstanding incidents of pioneer travel by land, sea and air in connection with medicinal and chemical products. At the central portion of the exhibit is situated a four-way automatic photographic projector which presents an entirely original method of projecting simultaneously on four screens, four different photographs, changing them automatically and continuously. The subjects projected appeal to all interested in photography, travel, medicine and first-aid.

The exhibit includes a model of the Research Institution, London, and displays from various laboratories, the museum and Wellcome activities throughout the world.

The influence of chemicals on modern civilization is graphically shown in the Mallinckrodt exhibit. Uses are shown of bismuth, copper, iodine, mercury silver and the products made from gallnuts. Displays indicate how crude material is transformed into fine chemicals; also pictorial presentation of some historical events in the development of medicine.

In commemoration of the founding of the Wm. S. Merrell Co., the grandsons and great grandsons of the founder have prepared an historical narrative of the development of the firm in which the historical events of the period from 1828 to 1930 are depicted. Accompanying the booklet is the rental agreement between Wm. S. Merrell and the owner of the building then occupied in the manufacture of pharmaceuticals. The monthly rental agreed upon was $6.50.

SOCIETIES AND COLLEGES.

SECTIONS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The program of the Madison A. PH. A. meeting should be printed in the next issue of the JOURNAL, request is therefore made that Section officers send in their reports promptly; accompanying titles of papers the authors are respectfully requested to include brief abstract, so these can be mimeographed and mailed to the pharmaceutical publications. Up to the present time titles of the Scientific Section and Section on Historical Pharmacy have been submitted.

It has been necessary to condense reports on colleges and defer publication of State Association Notes.

SCIENTIFIC SECTION.

1. "A Modified Assay Process for Alkali Benzoates and Salicylates," Jacob E. Schmidt and John C. Krantz, Jr.

2. "The Detection of Small Quantities of Carbon Monoxide in Medicinal Oxygen," Jacob E. Schmidt and John C. Krantz, Jr.

3. "A Note on the Water-Content of Magnesium Oxide," Jacob E. Schmidt and John C. Krantz, Jr.

4. "The Barbituric Acid Derivatives as Drugs," J. Howard Graham.

5. "Isolation and Identification of Sucrose from Senega," Ralph Bienfang.

6. "The Gravimetric and Volumetric Determination of Antipyrine as Hydroferrocyanide in the Presence of Pyramidone," I. M. Kolthoff.

7. "Tincture of Digitalis," L. W. Rowe and W. L. Scoville.

8. "Fluid Extract of Ergot," L. W. Rowe and W. L. Scoville.

9. "Licorice Fern and Wild Licorice and Substitutes for Licorice," Louis Fischer and E. V. Lynn.

10. "The Value of Senecio in Medicine," Edgar A. Kelly and E. V. Lynn.

11. "Two Species of Genus Ledum," Russell A. Cain and E. V. Lynn.

12. "What Is an Important Drug?" L. K. Darbaker.

13. "Some Plants of Western Pennsylvania Which Have Been Used in Medicine," L. K. Darbaker.

14. "Further Studies on Psyllium Seed," Heber W. Youngken.

15. "The Hyperglycemic Action of Forty Amines," Robert C. Anderson and K. K. Chen.

16. "Cod Liver Oil: Stability of Vitamin A Content under Conditions of Commercial Distribution," Geo. E. Ewe.

17. "A Study of the Constituents of Siam Benzoin in Relation to Their Preservative Action on Lard," William J. Husa & Donald E. Riley.

SECTION ON HISTORICAL PHARMACY.

1. "Henrik Ibsen—Pharmacist," Lt. Commander L. H. Roddis.

2. "Superstition, Credulity and Skepticism—Three Bugbears with Which Pharmacy Has Always Had to Contend," Charles Whitebread.

3. "C. Lewis Diehl," John E. Kramer.

4. "John Tennent and Seneca Rattlesnake Root," Ralph Bienfang.

5. "The Evolution of the Surgical Dressing, Bandages, etc.," F. B. Kilmer.

AMERICAN MEDICAL ASSOCIATION.

The American Medical Association held its annual meeting in Milwaukee beginning June 11th. Future policies governing many phases of medical practice were discussed. The retiring president of the Association is Dr. E. H. Cary, of Dallas, the president of the ensuing year is Dr. Dean Lewis, of Baltimore. The chairman of the Board of Trustees is Dr. A. R. Mitchell, of Lincoln, Nebraska, other members are: Drs. D. Chester Brown, Danbury, Conn., J. H. J. Upham, Columbus, O., Allen H. Bunce, Atlanta, Ga., Joseph A. Pettit, Portland, Ore., Rock Sleystea, Wauwatosa, Wis., Arthur W. Booth, Elmira, N. Y., Thomas S. Cullen, Baltimore; J. H. Walsh, of Chicago, is the *Secretary*.

JUNE STATE ASSOCIATION MEETINGS.

ALABAMA, 14th–16th, Mobile.
ARKANSAS, 13th–15th, Little Rock.
CALIFORNIA, 19th–22nd, Long Beach.
COLORADO, 13th–15th, Colorado Springs.
DELAWARE, 20th–22nd, Ocean City, Maryland.
FLORIDA, 20th–22nd, Tampa.
IDAHO, 26th–27th, McCall.
INDIANA, 20th–23rd, Lake Wawasee.
KENTUCKY, 20th–24th, Crab Orchard.
MAINE, 27th–29th, Rangeley.
MARYLAND, 20th–22nd, Ocean City.
MASSACHUSETTS, 12th–14th, Swampscott.
MISSISSIPPI, 19th–21st, Golden Anniversary, Jackson.
NEBRASKA, 6th–8th, Lincoln.
NEW HAMPSHIRE, 25th–27th, Portsmouth.
NEW JERSEY, 14th–16th, Asbury Park.
NEW YORK, 20th–23rd, Stamford.
NORTH CAROLINA, 20th–22nd, Charlotte.
NORTH DAKOTA, 13th–15th, Bismarck.
OHIO, June 25th–July 2nd, Cruise to Chicago World's Fair.
PENNSYLVANIA, 27th–29th, Bedford Springs.
SOUTH CAROLINA, 14th–15th, Greenville.
SOUTH DAKOTA, 26th–28th, Rapid City.
UTAH, 8th–9th, Salt Lake City.
VERMONT, 25th–27th, Lake Bomasseen.
VIRGINIA, 26th–27th, Virginia Beach.
WASHINGTON, 26th–28th, Sunrise Park, Mt. Rainier.
WEST VIRGINIA, 12th–13th, Clarksburg.
WISCONSIN, 27th–29th, Green Lake.
AMERICAN PHARMACEUTICAL MANUFACTURERS' ASSOCIATION—June 21st–24th, Chicago.

UNIVERSITY OF MARYLAND.

The following graduates of the School of Pharmacy, University of Maryland, received the Doctor of Medicine degree from the University at the exercises held at College Park on June 3rd: Joseph Cecil Bernstein, Jerome Fineman, Gustav Highstein, Wallace Henry Malinoski, Nathan Racusin, David H. Rosenfeld, Samuel Rubin, George Schochet, Paul M. Schwartz, Samuel Weisman. The latter was awarded the Dr. A. Bradley Gaither Memorial Prize for the best work in genito-urinary surgery during the senior year.

Frank L. Black, of Baltimore, was elected president of the Alumni Association for the ensuing year. A delightful entertainment program was carried out. Harry R. Rudy, Hagerstown, Md., presided as toastmaster; Rev. Oscar F. Blackwelder, well and favorably known to the radio audience, was one of the principal speakers.

TEMPLE UNIVERSITY.

The Commencement program of Temple University was of particular interest because of the conferring of the Doctor of Science degree on Secretary E. F. Kelly, of the AMERICAN PHARMACEUTICAL ASSOCIATION. Dr. Charles R. Mann, director of the American Council on Education, was honored with the degree of Doctor of Laws.

A delightful function was presided over by Dean H. Evert Kendig—a luncheon for the visitors and attended by members of the pharmaceutical faculty.

The Commencement Exercises were held in the Municipal Auditorium, with a seating capacity of 15,000, and few vacant seats. President Frank Aydelotte was the principal speaker. He urged that continuance of democracy and its protection against replacement by some form of dictatorship be safeguarded by greater use of experts in public affairs. But he warned that "the control of experts must be in the hands of laymen."

COLLEGE OF PHARMACY OF COLUMBIA UNIVERSITY.

The 103rd commencement of the College of Pharmacy of Columbia University was held May 24th at the McMillin Academic Theatre.

The exercises were conducted by the first vice-president of the College, Dr. Henry C. Lovis, who is retiring from active service at the close of the present academic year. The invocation and benediction were offered by the Reverend Wendell Phillips, Assistant Chaplain of the University. Dean H. V. Arny presented the candidates for degrees. Dr. William J. Schieffelin, honorary president of the College, addressed the graduates.

PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

The 111th annual commencement of the Philadelphia College of Pharmacy and Science was held June 7th. Special guests of honor at the alumni reunion this year were the graduates celebrating the fiftieth anniversary of their graduation; sixteen were present.

The following Alumni officers were elected: *President*, Joseph W. E. Harrisson; *First Vice-President*, Frank N. Moerk; *Second Vice-President*, John E. Kramer; *Recording Secretary*, Joseph W. England; *Treasurer*, Brua C. Goodhart; *Corresponding Secretary*, H. A. Rohn.

Following the annual meeting, ivy planting and plaque placing took place on the College grounds. An important feature of the afternoon ceremonies was the presentation by the class of 1887 of a mural which was the second of the series to be placed in the library. It is dedicated to the memories of John M. Maisch, Samuel P. Sadtler and Henry Trimble.

CONNECTICUT COLLEGE OF PHARMACY.

The Sixth Commencement exercises of the Connecticut College of Pharmacy were held on Monday evening, June 5th, at Sprague Memorial Hall, Yale University Campus, New Haven. Honorary degrees of Doctor of Pharmacy were conferred on Fred W. Lake and George L. Rapport. The address to the graduates was delivered by Dr. Robert P. Fischelis, on "Pharmacy's Contribution to Public Health Service."

MEDICAL COLLEGE OF VIRGINIA.

Dr. Julian A. Burruss, president, Virginia Polytechnic Institute, was the commencement speaker at the final exercises of the Medical College of Virginia, May 30th, including graduating classes in medicine, dentistry, pharmacy and nursing.

Dr. William deBerniere MacNider, Kenan Professor of Pharmacology, University of North Carolina Medical School, was awarded the honorary degree of Doctor of Science.

Portrait of Dr. Lewis Webb Chamberlayne, first professor of Materia Medica and Therapeutics, was unveiled.

ST. JOHN'S SCHOOL OF PHARMACY CHANGES NAME.

St. John's College, School of Pharmacy, will be known as the St. John's University College of Pharmacy, beginning with July 1st. Although not compulsory by the state curriculum, courses in English and Public Speaking, Pharmacy Clinic and Pharmacy Journal Seminar have been added with the view that such studies would enable the curriculum to strike a cultural balance.

OFFICERS OF CALIFORNIA COLLEGE OF PHARMACY STUDENT BRANCH.

President, John Isi.
Vice-President, Allen Caldeira.
Secretary, Eugene Bettencourt.
Treasurer, William Uomini.

PITTSBURGH.

The following interesting program for June 20th was carried out by Pittsburgh Branch, A. PH. A., at Hotel Schenley.

1. "Hobby" Exhibit at 7:45 P.M.
2. "St. Paul—Thorn in the Flesh and His Physician," by Dr. C. E. McCartney.
3. "The Place of the Physician in Cultural and Social History," by Dr. R. J. Ferguson, Associate Professor of History, University of Pittsburgh.
4. "Landmarks in the History of the Allegheny County Medical Society," by Theodore Diller, M.D.

C. T. VAN METER, *President*.

MEETING OF INTERNATIONAL PHARMACEUTICAL FEDERATION POSTPONED.

President J. J. Hofman and Secretary T. Patjewijd advise that the meeting of the International Pharmaceutical Federation, which was to be held in Prague has been indefinitely postponed.

OBITUARY.

EDWARD STRAHLMANN.

Edward Strahlmann, member of the AMERICAN PHARMACEUTICAL ASSOCIATION, died April 11th, aged seventy-three years. He was a native of Germany, and came to the United States at the age of fifteen. He graduated from the New York College of Pharmacy in 1880.

He came to San Francisco in 1875 and engaged in the drug business. In 1888 he opened a drug store in San Diego. Later he entered into partnership with E. Mayer under the firm name of Strahlmann-Mayer Drug Co. This store remained on the corner of 4th & Broadway for more than forty years. About four years ago the pharmacy was moved to its present location at Sixth and C Streets.

Mr. Strahlmann was a director of the First National Bank, and the Silvergate Building and Loan Company. He is survived by his widow, Mrs. Chrystal Strahlmann, two sons, Dr. Louis Strahlmann, Police Surgeon, and Otto Edward Strahlmann, Los Angeles.

The deceased was active in Association work for many years and highly regarded.

GUSTAV SCHERLING.

Gustav Scherling, veteran Sioux City druggist, died May 13th. He had been a member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1884.

Rev. Joseph Steele, Jr., officiated at the obsequies and members of Columbian Commandery, Knights Templar, served as an escort and members of Tyrian Lodge, A. F. & A. M. were in charge of services at the grave.

Mr. Scherling had operated a drug store at 1201 Fourth Street since 1890. For several years previously he had been a clerk for F. Hansen and S. H. Moore and in other Sioux City drug stores.

Born in Guttenberg, Ia., March 29, 1862, Mr. Scherling came to Sioux City as a young man. When he entered business for himself it was with Charles F. Arnold, a fellow graduate at the Philadelphia College of Pharmacy in 1883, under the firm name of Scherling and Arnold. They opened 43 years ago and Mr. Scherling was still in business at the same location at the time of his death. He took an active interest in the University of Iowa College of Pharmacy and ASSOCIATION promotions.

Survivors include his widow and one daughter, Mrs. Fred Schmidt of Sioux City.

EMIL LOUIS BOERNER.

Emil Louis Boerner, first dean of the College of Pharmacy of the State University of Iowa, died May 28th, aged seventy-eight years. A sketch and half-tone of the deceased appear in the August number, 1927, page 709. A brief reference to honors bestowed on him was printed in the January number of this year, page 71.

Mr. Boerner became a member of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1877, having graduated from the Philadelphia College of Pharmacy and Science in 1876. He was member of the Committee of the Iowa Pharmaceutical Association, which brought about the establishment of the Department of Pharmacy at the State University, of which he was a member of the faculty until 1904. In his opinion a pharmacist should practice pharmacy and not be deeply concerned in unrelated side lines.

Dr. Boerner is survived by his widow, a daughter, Mrs. Edward S. Rose, and two sons Robert H. and Fred W. Boerner.

DAVID M. FLETCHER.

David M. Fletcher, member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1904, died at his home in San Francisco after prolonged illness, May 21st. He was born in San Francisco, February 9, 1863; graduated from the University of California; thereafter he engaged in business on his own account until the earthquake in 1906 when he moved to Vallejo. In 1910 he accepted a position with the Owl Drug Company and, later, with Sure Drug Co. In 1922 he was appointed inspector for the State Board of Pharmacy and served until poor health necessitated his retirement. He is survived by his widow, a daughter, Mrs. Irwin Meyer, and a son, Dr. Charles Fletcher.

PARKER COOK.

Parker Cook, Life Member of the AMERICAN PHARMACEUTICAL ASSOCIATION, long prominent in drug and business circles, died at the Johns Hopkins Hospital, on June 6th, after an illness of some months' duration. Mr. Cook was born in Baltimore, February 16, 1875. He married Miss Henrietta McCrae, who died a few years ago. In 1893 he engaged with the late Captain Isaac E. Emerson, and was later associated in his various business projects. At the time of his death, Mr. Cook was vice-president of the Maryland Glass Company, and of Emerson's Bromo-Seltzer, Inc. He was a member of the executive committee of the Baltimore Trust Company, and held membership in the Maryland Club, University Club, Baltimore Country Club, and also was a member of the Metropolitan and Army and Navy Clubs in Washington. The deceased was a thirty-second degree Mason and a member of the Shrine.

Mr. Cook had long been an active member of the Maryland Pharmaceutical Association, and served as a member of the Committee on Legislation for many years.

JAMES ANDERSON YATES.

Dr. J. A. Yates of Edmonton, Ky., member of the AMERICAN PHARMACEUTICAL ASSOCIATION, died March 26th. Aside from his interests in pharmacy, he was a practicing physician and held in highest regard by the community. Dr. Yates was born September 29, 1860. For fifty years he was engaged in the practice of medicine and eighteen years as a registered pharmacist and served thirty years as health officer of Metcalf County. H. H. Hurst succeeds Dr. Yates as pharmacist.

The deceased stood high as a citizen and was active in Masonry. Resolutions of respect were passed, testifying that "in the passing of Dr. Yates, Edmonton had lost one of the most faithful and devoted members of the Masonic bodies, and the community a good citizen and beloved physician, and his family a devoted husband and father."

The deceased is survived by his widow.

The 3-year old son of Professor and Mrs. J. Lester Hayman of Morgantown, W. Va., was struck by an automobile on June 2nd, death resulting almost instantly. Professor Hayman is well and favorably known as secretary of the West Virginia Pharmaceutical Association. Sympathy is expressed.

FRESCOS IN DETROIT INSTITUTE OF ARTS.

Among the frescos representing Detroit industries recently given to the Institute of Arts of that city, by Edsel Ford, are two of interest to pharmacists. They are the work of Diego Rivera, well-known muralist, and took approximately eight months to complete. One depicts "Vaccination" and shows a child being vaccinated in a serum laboratory. In the foreground are shown serum-giving animals. Another shows an interior view of the pharmaceutical plant of Parke, Davis and Company.

LEGAL AND LEGISLATIVE.

NARCOTICS CONVENTION ACTION IS TO BE EFFECTIVE JULY 10TH.

The Department of State is informed that ratifications of the Narcotics Limitation Convention of 1931 had been deposited April 10th with the Secretariat of the League of Nations by twenty governments and accessions by nine. Under the terms of the convention, it is to come into force ninety days after the Secretary-General of the League of Nations has received the ratifications or accessions of twenty-five states, which must include at least four of eight specified manufacturing nations. The convention will, therefore, go into force July 10th, in respect of the twenty-nine nations referred to above.

The manufacturing nations which have now ratified or acceded are: France, Germany, Great Britain, Turkey and United States of America.

The other nations which have ratified or acceded are: Brazil, Canada, Chile, Cuba, India, Italy, Mexico, Monaco, Portugal, Spain, Sweden, Uruguay, Belgium, Dominican Republic, Egypt, Lithuania, Bulgaria, Costa Rica, Nicaragua, Persia, Peru, Sudan, Salvador, Hungary.

This convention is confidently expected to constitute an effective and important step in the direction of suppressing the evils of the illicit drug traffic and of reducing the production of narcotic drugs to the amounts needed for medical and scientific purposes.

TRADE-MARKS FOR DRUGS DEMANDED BY SIROVICH BILL.

The *Oil, Paint and Drug Reporter* of June 19th states:

"Interstate commerce would be closed to drugs, antiseptics, cosmetics, dentifrices and beverages which are not labeled with a registered trade-mark, by the terms of a bill (H. R. 6118) introduced by Representative William I. Sirovich, a New York physician.

"This measure would prohibit the interstate shipment of the articles named, whether they be simple substances or compound preparations, which had not been trademarked and which did not contain on the label a statement of its quantitative composition and of the properties of the components."

The Sirovich bill has been referred to the House Committee on Patents. The first section follows:

A BILL.

To provide for the truthful labeling of drugs and the attachment of trade-marks to the containers and packages of drugs.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled. That after the passage of this act every individual container or package of all drugs transported, shipped or sold in interstate commerce shall have affixed thereon a label, which label shall state the names and composition of the drugs contained therein, including the ingredients, the properties and proportions of each drug in the composition or compound or combination, which label shall also bear a trade-mark registered in the United States Patent Office under the act of February 20, 1905, or the act of March 19, 1920, but it shall be considered compliance with the requirements of this act if instead of a registered trade-mark there be affixed to each container or package a notice of an application to register a trade-mark that has been filed in the United States Patent Office within thirty days of the passage of this act or within thirty days of the adoption and use of the trade-mark in interstate commerce: Provided, however, That any trade-mark the registration of which has been finally refused shall not be affixed to any container or package of drugs transported, shipped or sold in interstate commerce.

Section 6 reads in part:

Section 6. The term "drug" as used in this act shall include all medicines and preparations recognized in the United States Pharmacopœia or National Formulary for internal or external use and any substance or mixture of substances or combination of substances intended to be used for the cure or mitigation or prevention of disease of every man or other animals, and all cosmetics, beverages, antiseptics and teeth-cleansing preparations.

BOOK NOTICES AND REVIEWS.

The Vitamins in Health and Disease. By BARNETT SURE, Ph.D., Professor of Agricultural Chemistry, University of Arkansas, Fayetteville, Arkansas. April 1933, pages xiv + 206, 4 tables. Price $2.00. Publishers, The Williams & Wilkins Company, Baltimore, Maryland.

There are several texts which discuss the properties of vitamins, chemical procedures used in isolation and identification and general methods of testing for the presence or absence of these essential constituents in various food stuffs.

The necessity for the inclusion of adequate amounts of the various vitamins in our diet has been stressed. They are essential for reproduction, milk secretion, appetite, bone and tissue building, growth, resistance to an infection, dentition, etc., etc.

Doctor Sure has written a very interesting book in non-technical language in which the discovery of vitamins, and their necessity in the diet are discussed as a basis for presentation of the effects observed when the diet is deficient. Vitamins A, B, C, D, E and G are each presented for our consideration, their occurrence mentioned and the effect on animals and on humans following the consumption of inadequate quantities very clearly presented. One chapter deals with the vitamin content indicating the particular foods which are rich, as well as the particular foods which are poor in each vitamin. A diet is given which will ensure an adequate amount of vitamins, for infants as well as for adults. The reason for the development of vitamin concentrates, and the rôle of vitamins in health and in disease is very effectively presented. The book closes with the suggestion that by proper attention to diet, including optimum vitamin content, we can help the present situation in which almost one-half of our population are physically imperfect and 3,000,000 people annually are seriously ill. Dr. Sure has presented a readable and interesting discussion of this important problem.—JAMES C. MUNCH.

The Mode of Action of Drugs on Cells. By A. J. CLARK, B.A., M.D., F.R.C.P., F.R.S., Professor of Materia Medica in the University of Edinburgh, formerly Professor of Pharmacology in the Universities of London and Cape Town. Author of "Applied Pharmacology," 1933, pages vii + 298, 62 figures. Price $6.25. Publishers, Williams and Wilkins Company, Baltimore, Md.

So much attention has been directed to the qualitative action of drugs (pharmacology), in order to establish this as a science, that our attention has not been concentrated on the quantitative measurements of drug action (bioassays). It is, therefore, very timely to pause and consider just how much information we have regarding the mode of action of drugs on cells and the proper mathematical or statistical consideration of pharmacological data. Within the last five years papers have begun to appear dealing with the statistical consideration of pharmacological data. "The majority of pharmacological data expressing equilibria between drugs and cells approximate to an exponential form." Unfortunately, there has been a tendency to obscure the inherent variations in pharmacological data and hide our ignorance behind a formula, which may or may not have any relation to the law governing drug action.

Dr. Clark has rendered a real service in pointing out the necessity for consideration of proper statistical treatment. In the thirteen chapters of this book the living cell is considered as a physical chemical system, fixation of drugs considered in the light of physical laws, the mechanics of equilibria discussed, various theories regarding the action of drugs presented and used to account for the mode of action of various hormones as well as vitamins; drug antagonism and temperature effects as well as the action of radiation on living cells are presented.

The mathematics are presented in a very interesting fashion and serve as a basis for a conclusion "that the only studies in quantitative pharmacology that are likely to yield results of theoretical interest are those made on the very simplest systems."

Considered from the philosophical standpoint, evidence is presented that "the simplest probable conception of drug action is that potent drugs occupy certain specific receptors on the cell surfaces, and that these specific receptors only comprise a small fraction of the total cell surface." This concept has been adapted from studies in physical chemistry and serves to explain very plausibly some of the rather startling figures: ouabain fixed by a frog heart cannot cover more than 3 per cent of the surface of the cell; the amount of lysin reacting with a human erythrocyte is just sufficient to cover the cell surface with a monomolecular layer; the protein content of

the smallest micro-organism compatible with life is that limit required to form a monomolecular surface layer; a man weighing 70 kilos has 26 times 10^{12} cells, so a daily maintenance dose of calciferol (vitamin D concentrate) of 0.1 gamma per kilo will supply 100 molecules to every cell in the body; the product of light activation in the retina is more potent than any known hormone; the toxicity of thallium sulphate for rats can be measured with a probable variation of 17 per cent, ouabain 8.3 per cent, adrenalin 71 per cent on mice.

A careful study of this book will dispel many of the wild notions and foolish theories encountered in some of the current literature. This book will prove very useful to all students of drug activity.—JAMES C. MUNCH.

PUBLICATIONS RECEIVED.

A Model Code for Self-Governing Industries, under the National Industrial Recovery Act, DR. A. P. HAAKE. Issued by the National Association of Manufacturers. Single copies may be obtained free—address Union Trust Building, Washington, D. C., or 11 West 42nd St., New York City.

Merck & Co. have published an illustrated booklet marking the occasion of the opening of their Research Laboratories. It contains also addresses delivered during the dedication ceremonies.

Manual of Pacific Coast Drug Plants. By ERNST T. STUHR. Author of Medicinal Plants of Florida, Native Drug Plants of Nebraska, Medicinal Trees of the U. S. A., Oregon Drug Plants. Science Press, Lancaster, Pa. Price $2.65.

This *manual* is a handsome Morocco (semi-flexible) bound volume, recording over eleven hundred plant species.

A consideration of the medicinal plants thriving throughout the Pacific slope states—presenting the scientific and common names, part used, therapeutic uses and approximate range of the respective plants. Especially adapted as a reference of existing economic plants.

The Economic Aspects of Medical Services. The University of Chicago Press, Chicago, Ill. A reprint, with slight condensation, of Chapters 34 and 35 of "The Costs of Medical Care," by I. S. Falk, C. Rufus Rorem and Martha D. Ring (The University of Chicago Press, 1933). This volume, which is Publication Number 27 of the Committee on the Costs of Medical Care, is a summary of all of the Committee's studies as well as of other investigations in this field. It does not contain the recommendations of the Committee. These appear in the "Final Report," Publication Number 28.

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